

Fractional laser and low-level light combination therapy in patients with recalcitrant alopecia areata

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Background and Objectives

The current treatment options for alopecia areata (AA) typically aim to suppress inflammatory T-cell responses. Patients vary in their response to these treatments, and some do not respond to one or more types of therapy. Herein, we report the outcomes of combination therapy, employing fractional laser treatment and low-level light therapy (LLLT), with a focus on patients with recalcitrant AA.

Materials and Methods

LLLT (HEALITE II®; Lutronic, Goyang, Republic of Korea) and fractional laser treatment (Starlux™ 1540; Palomar Medical Technologies Inc., Burlington, MA, USA) were administered to the subjects every two weeks. Two dermatologists independently compared photographs taken at baseline and final follow-up visits and assessed the level of hair regrowth using a 5-point scale. The scale levels and their description are as follows: 0, no improvement; 1, < 25% (slight improvement); 2, 25%-50% (moderate improvement); 3, 50%-75% (marked improvement); and 4, 75%-100% (most improvement).

Results

Twenty patients (13 males and 7 females) were evaluated in this study. The mean improvement level was 2.55 points with 55% (n = 11) of patients showing > 50% improvement. No serious adverse events occurred, and treatment cessation was never deemed necessary.

Conclusion

Based on the results of this study, we propose that combination therapy may represent a viable new approach for the treatment of recalcitrant AA.

Key words

Fractional photothermolysis; Low level light therapy; Alopecia areata

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INTRODUCTION

The management of alopecia areata (AA) depends on the age of the patient as well as the extent, activity, and duration of the disease. Topical therapy, including topical steroids combined with topical minoxidil and steroid injections can be used in certain cases, including mild cases.¹⁻³ In severe cases, which are accompanied by rapid, extensive hair loss ($\geq 50\%$), the administration of more aggressive therapies are necessitated; such therapies typically include the systemic administration of immunosuppressive agents (e.g., cyclosporine, azathioprine, methotrexate, and JAK/STAT inhibitors) and topical immune-modulators.⁴⁻⁸

Arguments favoring the use of systemic immunosuppressive agents highlight their efficacy in the treatment of patients experiencing their first episode of hair loss, those who have experienced ≤ 12 months of hair loss, and those with $< 50\%$ hair loss; counter-arguments highlight the tendency to relapse after stopping immunosuppressive administration.⁹ Indeed, 14% to 100% of patients relapse within 4 to 9 weeks after discontinuing steroids. Additionally, side effects associated with the systemic administration of steroids occur in 30% to 40% of patients; this generally precludes their long-term use. Known side effects include suppression of the pituitary-adrenal axis, effects on bone growth or integrity, changes in vision and mood, and the exacerbation of hypertension and diabetes.

These noted shortcomings of the approaches prompt the development of safe, alternative therapeutic ap-

proaches that produce sustainable hair regrowth without permanent side effects. Recent research has examined whether low-level light therapy (LLLT) and fractional laser treatments, with or without the addition of topical agents, represent safe and effective alternative treatment options.¹⁰⁻¹⁶ Since then, several studies have been published on AA treatment using fractional lasers.¹⁷⁻²⁵

In this study, we detail our experience in treating patients with recalcitrant AA using fractional laser and LLLT combination therapy and discuss the treatment outcomes.

MATERIALS AND METHODS

Patient selection

A retrospective chart review was performed on patients with recalcitrant AA who visited the Chung-Ang University Hospital between 2019 and 2021. This study was approved by Chung-Ang University Hospital's institutional review board (CAUHS19907). All subjects in this study were signed written informed consent before submitting this paper. Recalcitrant AA was diagnosed in the clinic according to the following criteria: (1) lesions covering less than 50% of the scalp, (2) no response to previous therapies on lesions present for more than 6 months, and (3) no hair regrowth over the past 12 months without treatment. The exclusion criteria were as follows: (1) lesions covering more than 50% of the scalp and (2) the presence of alopecia totalis or universalis.

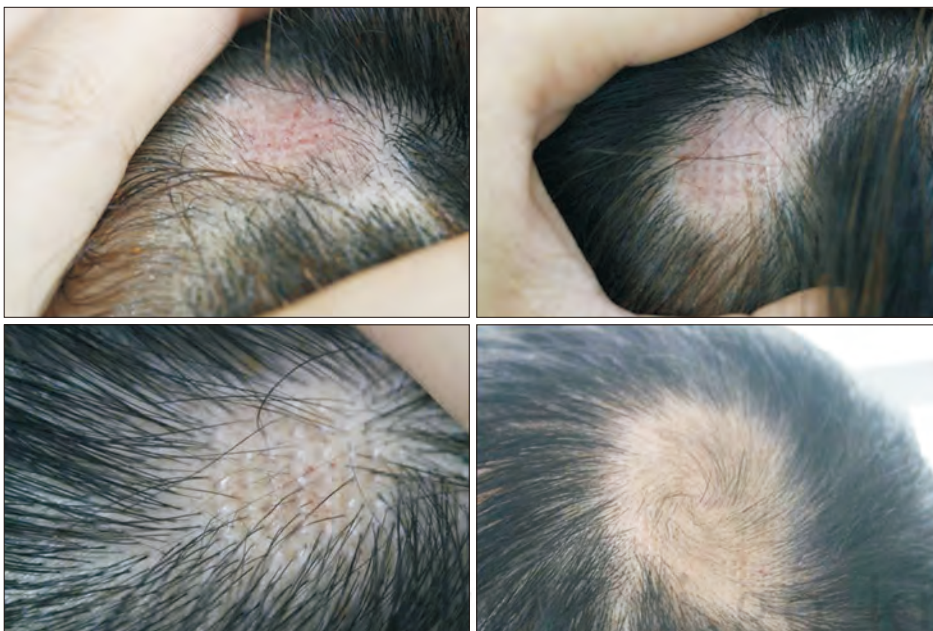


Fig. 1. Response and condition immediately following fractional laser treatment of recalcitrant alopecia areata.

Treatment methods (low-level light therapy & fractional laser treatment)

LLLT and fractional laser irradiation were performed every two weeks. The LLLT device was operated with the following parameters: 830 nm LLLT (HEALITE II®; Lutronic, Goyang, Republic of Korea) with a concomitant power density of 4 J/cm² and an 800 seconds duration of application. The recommended distance between the lesion and the LLLT device was 150-200 mm. Fractional laser treatment was administered using a 1,540 nm fractional laser system (Starlux™ 1540; Palomar Medical Technologies Inc., Burlington, MA, USA) with a pulse energy of 30 mJ, a duration of 15 ms, a 100 MTZ/cm²/pass density, and two passes (Fig. 1).

Evaluation

Responses to treatment were assessed via clinical examination and digital photography. Two dermatologists independently compared photographs from the baseline and final follow-up visits and assessed the level of hair regrowth using a 5-point scale. The scale levels and their interpretations are as follows: 0, no improvement; 1, < 25% (slight improvement); 2, 25%-50% (moderate improvement); 3, 50%-75% (marked improvement); and 4, 75%-100% (most improvement). More current scoring systems for AA (The severity of alopecia tool [SALT] I and II) were not used in this study. All adverse events that occurred during treatment were recorded.

RESULTS

Twenty patients were evaluated in this study (13 male and 7 female). The mean age of the patients was 44.84 years (range, 29-66 y), and the mean disease duration was 9.2 months (range, 6-24 mo). A single lesion was observed in only one patient (5%), and 19 patients (95%) presented with multiple lesions; the average lesion count was 6.85 (range, 1-12). Patients' demographic information and results are presented in Table 1.

The grading scale scores were 4 points (most improvement) for five patients (25%, Fig. 2), 3 points (moderate improvement) for six patients (30%, Fig. 3), 2 points (moderate improvement) for five patients (25%, Fig. 4), 1 point for three patients (15%, Fig. 5), and 0 points for one patient

Table 1. Patients' demographic details

Characteristic	Value
Age (y)	44.85 (29-66)
Sex (male/female)	13/7
Duration of AA (mo)	9.2 (6-24)
Numbers of lesions	6.85 (1-12)
Lesion	
Solitary	1 (5)
Multiple	19 (95)
Ophiasis	3 (15)
Recurrence history of AA	4 (20)
History of AD	3 (15)
History of autoimmune	1 (5)

Values are presented as mean (range), number only, or number (%). AA, alopecia areata; AD, atopic dermatitis.



Fig. 2. Clinical photographs of patients with recalcitrant alopecia areata, representative of patients with scores of 4 (most improvement).



Fig. 3. Clinical photographs of patients with recalcitrant alopecia areata, representative of patients with scores of 3 (marked improvement).

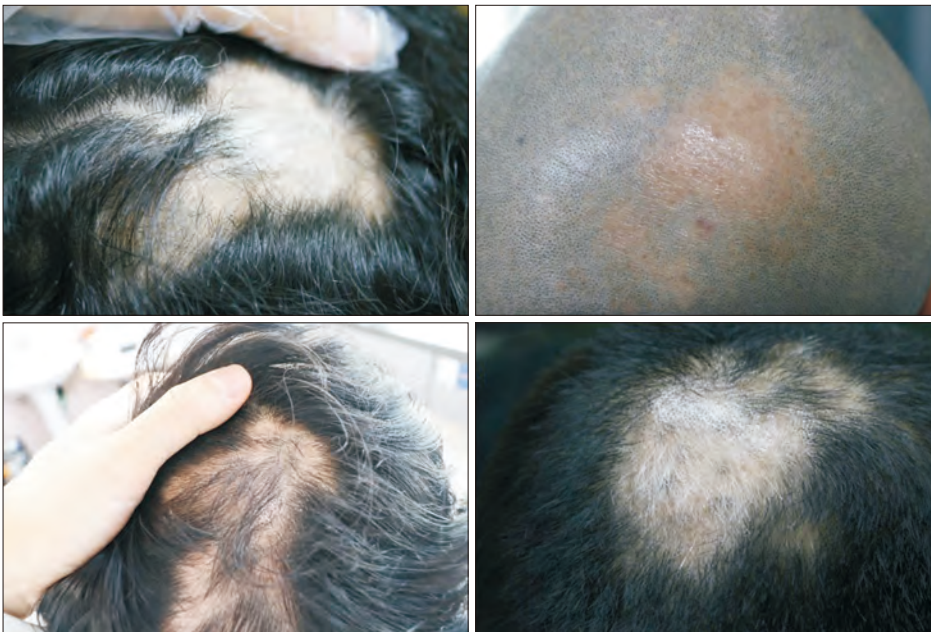


Fig. 4. Clinical photographs of patients with recalcitrant alopecia areata, representative of patients with scores of 2 (moderate improvement).

(5%). The mean improvement score was 2.55 (Table 2).

No significant adverse effects were noted in any of the treated patients; all patients tolerated the procedure well. No patients showed any evidence of skin atrophy in the treated area during the follow-up period. Temporary pain was the only side effect observed following fractional laser treatment and this was well tolerated. No sedation or other medication was required during the procedures.

DISCUSSION

Previously, LLLT has been successfully used to treat AA. In one study, various wavelengths of LLLT were used to stimulate human dermal papilla cells, resulting in an increased hair follicle count and improved hair tensile strength.²⁶ These findings indicate that inflammation al-

leviation and immunological response modulation are potential mechanisms through which LLLT stimulates hair growth in patients with AA. In vitro and in vivo LLLT trials have resulted in reduced proinflammatory cytokine expression and increased anti-inflammatory cytokine production. The mechanism behind LLLT's function in the treatment of recalcitrant AA may also involve inflammation reduction.²⁷ Another advantage of LLLT is its synergistic effect, which increases the efficacy of topical agents. Some researchers have reported that the effects of LLLT in AA were reinforced by the topical application of minoxidil in rat models.²⁸

One proposed mechanism, through which fractional laser treatment may induce hair regrowth in recalcitrant AA, involves thermal injury, which may initiate hair follicle neogenesis from non-follicular stem cells. This treat-



Fig. 5. Clinical photographs of patients with recalcitrant alopecia areata, representative of patients with scores of 1 (slight improvement).

Table 2. Results of the outcome analysis

Score of response to treatment	Number of patients (%)
0	1 (5)
1	3 (15)
2	5 (25)
3	6 (30)
4	5 (25)
Mean score	2.55

ment can stimulate hair growth by creating microscopic thermal columns in the dermis, which induce wound healing. The thermal wounds created by fractional laser treatment may activate the *Wnt* pathway, which induces hair regrowth. Similarly, fractional laser treatment promotes increase in hair density, hair thickness, and the anagen/telogen ratio, thereby increasing the rate of hair regrowth.²⁹ Other possible mechanisms include the alteration of the microenvironment and alterations to local immune cells. The release of various chemokines potentially allows for the displacement of perifollicular infiltrates to other areas of the dermis and epidermis, and the redistribution of peribulbar T lymphocytes to the dermis and interfollicular epidermis. The “scattering of peribulbar lymphocytes” phenomenon may halt disease progression.¹⁷ Laser light has also been proposed to induce apoptosis in lymphocytic cells, mitigating the immune-cell-mediated destruction of follicles.²⁰

In this study, we evaluated the efficacy of combination therapy of fractional laser treatment and LLLT, performed at 2-week intervals, for treating recalcitrant

AA. The mean improvement score was 2.55, and many patients showed relatively high improvement scores, with 55% (11 patients) of patients showing an improvement of 50% or more (Table 2).

Fractional laser treatment is preferable to other laser treatments as it is less damaging to normal terminal hairs. Fractional lasers have no affinity for melanin and therefore cannot cause hair ablation. Another advantage of fractional laser treatment is the reduction in the incidence of skin atrophy with the over-use of topical steroids and steroid injections. However, if set to excessive energy levels or used with higher-than-recommended frequency levels, fractional lasers can worsen alopecia by stimulating fibrotic changes.³⁰ Therefore, promoting proper wound healing to induce hair growth with few side effects remains a problem.

Our study has some limitations. First, without a control group, the possibility of spontaneous hair regrowth could not be precluded. Further trials should include a control group to confirm the therapeutic effects of LLLT and fractional laser treatment. Second, the sample size was small, which makes it difficult to generalize the results to the entire population.

In conclusions, the treatment of recalcitrant AA remains challenging given the suboptimal efficacy rates of currently available treatments, and there is a need for highly effective treatment options. Based on the results of this study, we propose that our combination laser therapy could constitute a new approach for the treatment of recalcitrant AA. However, further research is needed to

examine the mechanism by which the employed lasers modify the immunology of the scalp to treat the disease. Research on LLLT and fractional laser treatment for AA remains preliminary, and additional studies are necessary to determine the viability of these approaches.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTIONS

Concept and design: KHY, BJK. Analysis and interpretation: JS, SYC. Data collection: JS, SYC. Writing the article: KHY, BJK. Critical revision of the article: KHY, BJK. Final approval of the article: KHY, BJK. Statistical analysis: JS, SYC. Overall responsibility: KHY, BJK.

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