



A novel 311-nm Titanium:Sapphire laser therapy for alopecia areata: a pilot study of 19 patients

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Received: 17 July 2019 / Accepted: 23 September 2019
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Introduction

Alopecia areata (AA) is an autoimmune skin disorder causing hair loss, thus, often negatively impacting patients' quality of life. Current treatment modalities for AA consist of intralesional corticosteroid injection, topical immunotherapy, and topical and systemic corticosteroids, but have substantial disadvantages such as the injection-associated pain, allergic sensitization, and various adverse effects [1]. Laser treatment using a 308-nm excimer laser (EL) has been reported to have benefits in treating AA with a non-pharmaceutical manner [2]. A recently introduced gain-switched 311-nm Titanium:Sapphire laser (TSL) has been used in the treatment of vitiligo, with a therapeutic efficacy similar to that of EL [3, 4]. Thus, in the present study, we evaluated the effectiveness and safety of the 311-nm TSL in the treatment of AA.

Methods

This open trial enrolled patients diagnosed with AA between May 2017 and December 2018. The alopecic lesions were treated once or twice weekly using a gain-switched 311-nm TSL (Pallas; Laseroptek, Seongnam, Korea). The initial treatment dose was 300 mJ/cm², with a 50 mJ/cm² increase at each subsequent session and continuing until post-treatment erythema occurred. In some patients, prior medical treatments were

not discontinued to maintain the existing therapeutic effect. The final analysis included patients who had undergone at least ten treatment sessions of TSL. Two dermatologists independently compared the photographs of the baseline and final follow-up and assessed the level of hair regrowth using a quartile grading scale (no regrowth, 0%; mild, 1–24%; moderate, 25–49%; good, 50–74%; excellent, 75–99%; complete, 100%). This study was approved by our institutional review board (VC19RESI0033).

Results

The 19 AA patients (10 women and 9 men) enrolled, including three with alopecia totalis (AT), had a median age of 39 years (range, 3–68) (Table 1). Nine patients had not responded to previous conventional treatments prior to enrollment. The median maximum dose was 700 mJ/cm² (range, 300–1650). Fourteen patients (73.9%) showed excellent to complete hair regrowth after a median of 14 treatments (range, 10–34) for 3.5 months (range, 2–8) (Fig. 1). One of them was AT patient (Fig. 2). Of the remaining 5 patients, 3 showed good ($n = 1$) or moderate ($n = 2$) hair regrowth whereas the remaining two patients, both of whom had AT, did not respond to treatment. Five patients (26.3%) experienced persistent erythema lasting > 48 h, but it improved spontaneously within a few days. No serious adverse events requiring treatment cessation occurred

Discussion

In this pilot study, a remarkable response to 311-nm TSL was achieved in 73.9% of the treated AA patients, including one of the three AT patients. Except for the occasional occurrence of self-resolving persistent erythema, treatment was well-tolerated. Moreover, our study included two children under the age of 10, and they and their parents were very satisfied with the

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Table 1 The treatment parameters and clinical outcomes of 19 patients with alopecia areata who underwent the Titanium:Sapphire laser therapy

No.	Sex/age (years)	Subtype	Disease duration (months)	Previous treatment	Response to the previous treatments	Accompanying treatment	Session of TSL therapy	Duration of TSL therapy (months)	Maximal dose (mJ/cm ²)	Level of hair regrowth ^a
1	M/15	pAA	1	None	NA	None	14	2	750	Complete
2	F/8	pAA	6	TCS	No response	TCS	11	2	700	Complete
3	M/42	pAA	3	TCS	No response	TCS	22	6	1650	Complete
4	F/36	pAA	2	None	NA	None	12	3	500	Excellent
5	F/12	AT	1	None	NA	SCS, TCS	12	2	800	No
6	M/68	pAA	2	None	NA	TCS	10	2	420	Good
7	F/37	AT	144	DPCP, ILI, SCS, TCS	No response	None	26	8	900	No
8	M/44	pAA	4	ILI, TCS	No response	TCS	14	7	800	Excellent
9	F/64	pAA	2	None	NA	None	12	3	400	Excellent
10	M/57	pAA	2	None	NA	None	16	4	350	Excellent
11	F/3	pAA	1	None	NA	None	14	2	450	Moderate
12	M/41	pAA	6	ILI, TCS	No response	TCS	13	4	600	Excellent
13	F/28	AT	252	DPCP, ILI, SCS, TCS	Response, but recurred	None	30	7	800	Complete
14	M/13	pAA	12	None	NA	None	34	8	1100	Excellent
15	F/53	pAA	2	ILI, TCS	No response	TCS	12	2	800	Moderate
16	F/12	pAA	6	TCS	No response	None	21	6	900	Excellent
17	F/65	pAA	1	None	NA	None	16	2	700	Excellent
18	M/39	pAA	3	ILI, TCS	No response	TCS	11	3	450	Excellent
19	M/56	pAA	1	None	NA	None	10	2	300	Complete

AT, alopecia totalis; DPCP, Diphenylcyclopropenone; ILI, intralesional injection; NA, not applicable; pAA, patch alopecia areata; SCS, systemic corticosteroid; TCS, topical corticosteroid

^a Level of hair regrowth: no regrowth, 0%; mild, 1 to 24%; moderate, 25 to 49%; good, 50 to 74%; excellent, 75 to 99%; complete, 100%

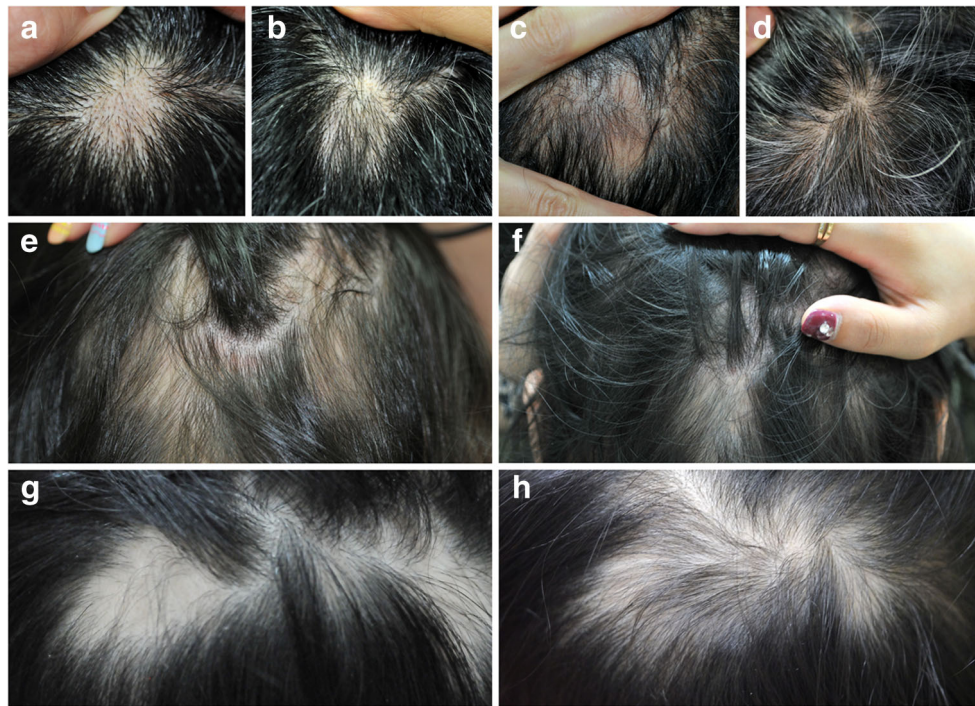


Fig. 1 Alopecia areata treated with with a gain-switched 311-nm Titanium:Sapphire laser. **a** A 41-year-old male (patient 12) with 6-month duration of alopecia areata before treatment. **b** After 13 treatment sessions, complete hair regrowth was observed (patient 12). **c** A 56-year-old male (patient 19) with a 1-month duration of alopecia areata before treatment. **d** After 10 treatment sessions, excellent hair

regrowth was observed (patient 19). **e** A 36-year-old female (patient 4) with 2-month duration of alopecia areata before treatment. **f** After 3 months with 6 treatment sessions, excellent hair regrowth was observed (patient 4). **g** An 8-year-old female (patient 2) with 6-month duration of alopecia areata before treatment. **h** After 2 months with 11 treatment sessions, complete hair regrowth was observed (patient 2)

TSL treatment with no risk of systemic adverse events and no treatment pain.

Although the mechanism by which TSL induces hair regrowth in AA has yet to be investigated, it seems to be related to the photobiological effects of modulating the immune

response, such as NBUVB, which emits a 311 nm as a peak wavelength. EL that emits a wavelength of 308 nm adjacent to 311 nm is expected to induce cutaneous immunosuppression, and reported to be effective in the treatment of AA. EL not only induces apoptosis in autoreactive T cells but also affects

Fig. 2 Alopecia totalis treated with a gain-switched 311-nm Titanium:Sapphire laser. **a** A 27-year-old female (patient 13) with a 21-year history of alopecia areata before treatment. **b** The regrowth of all hair was evident after 12 treatment sessions (3 months). **c** Full regrowth was achieved after 30 sessions (7 months)



immune reactions beyond the irradiated lesions by reducing circulating interleukin-17 levels and restoring regulatory T cell populations [5]. In a recent study of the use of EL in the treatment of vitiligo, stimulation of the Wnt/ β -Catenin signaling pathway was demonstrated [6] and may also participate in the induction of hair regrowth in AA patients. It is assumed that the TSL also induces hair regrowth of AA with similar mechanisms as ELs, but the mechanism needs to be clarified in future studies.

Our work had several limitations. First, there was no untreated control group to rule out the possibility of spontaneous hair regrowth. Since it was the first pilot study using a novel laser, we did not set up a control group. Further controlled trial with a sham control group should be conducted to clarify the therapeutic effect of TSL. Second, some patients who used topical corticosteroid prior to enrollment were allowed its continuous use during the study, which may have affected the outcome. However, since TSL was additionally performed on patches that had no response to previous treatments, most of the hair regrowth observed in our study is presumed to be due to the therapeutic effect of TSL.

We found the effectiveness and safety of TSL treatment in patients with AA. The 311-nm TSL provides a non-invasive, pain-free treatment for AA patients without any risk of adverse drug reactions and can be safely treated at various ages. It would be promising for AA patients, especially for children who are concerned about painful procedure. Because 311-nm TSL has a longer wavelength than 308-nm EL, it may penetrate deeper to the level of the hair bulb in the skin. Further controlled trials are needed to confirm our findings.

Funding information This work received financial support from the St. Vincent's Hospital, research institute of medical science (SVHR-2019-09).

Compliance with ethical standards The study protocol was designed in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Catholic Medical Center Office of Human Research Protection (VC19RESI0033).

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

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