Section A-Research paper



# Fractional Erbium YAG laser followed by topical clobetasol propionate versus Fractional Erbium YAG laser alone in the treatment of alopecia areata: a prospective randomized clinical trial

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Authors have no conflict of interest Funding statement: No funding received

Main text word count: 3000 words Tables: 5 Figs: 4

Contribution: All authors contributed equally in producing the work.

Data is available upon request from contact author

Short title: Fractional laser and topical steroid in AA

Keywords: Erbium: YAG laser, Clobetasone propionate, Alopecia

Section A-Research paper

#### Abstract

Introduction Alopecia areata (AA) is a non-scarring, inflammatory condition characterized by loss of hair of the scalp and/or body. Objectives Novel alopecia areata therapeutic methods have being developed in order to improve care quality. This study will compare the fractionaed Er: YAG laser alone versus fractionated Er: YAG laser accompanied by local steroid in the treatment of alopecia areata. Methods Thirty people with alopecia areata participated in the study. In each participant, one lesion was handled by fractionated Er: YAG laser (laser group) and another one by fractionated Er: YAG laser followed by local clobetasol propionate (combined therapy group). The Severity of Alopecia Tool (SALT) score, satisfaction of participants, and dermoscopic signs were used to assess therapy response. Results Both treatment modalities resulted in a statistically significant decrease in the SALT score and a significant clinical improvement in alopecia areata. Concerning the combined therapy group, the SALT score was higher. When making comparisons of dermoscopic signs of treated areas pre and post therapy, both modalities reported a significant reduction in all alopecia areata dermoscopic signs. Conclusion Fractionated Er: YAG laser with local corticosteroids has been proved to be efficient treatment modality in alopecia areata.

Keywords: Alopecia areata, fractionated Er:YAG laser, local steroid.

## Introduction

Alopecia areata (AA) is a non-scarring form of hair loss caused by an autoimmune disorder of the follicles. It could be a single patch or several patches that cover the entire scalp or cause total hair loss across the body [1]. Because its clinical course is unpredictable, it always results in substantial psychological suffering. Despite its high prevalence and extensive research, its

#### Section A-Research paper

exact cause is still unknown, and it has a high relapsing rate [2]. For localized scalp alopecia areata, topical corticosteroid therapy is considered the drug of choice. Alopecia areata has been treated with alot of topical corticosteroids in the form of creams and ointments [3].

Triamcinolone acetonide is the most used intralesional corticosteroid. Preferred concentrations for the scalp and face are 5mg/mL and 2.5mg/mL, respectively. Every 4 weeks, 0.1ml is injected for 1 cm<sup>2</sup>. Skin atrophy and telangiectasia are the most common side effects [4].Topical extremely potent corticosteroid under occlusion is recommended. For pediatric AA local steroids are more preferable as they reduce steroid effects and lessen inflammation.<sup>5</sup>

Because of the adverse effects of intralesional steroid (telangiectasia and skin atrophy); fractionated laser was found to be a more favorable procedure in which laser light promote hair regrowth.<sup>6</sup> Firstly they can promote apoptosis of T-lymphocytes infiltrating around the hair follicle and peribulbar lymphocyte reducing inflammation.<sup>7</sup> Moreover fractional lasers induce telogen to anagen transition by inducing a plethora of vascular circulation. Thirdly they maintain a speedy process of wound repair mediated by microthermal zone and heat shock protein release. Finally they improve transdermal dermal delivery of applied topical steroids and can maximize their effect.<sup>7</sup>

The purpose of this study is to compare the efficiency of fractionated erbium:YAG laser alone versus fractionated erbium:YAG laser with local clobetasol propionatein the management of AA.

#### Patients and methodology

## Study design

5363

In the period from August 2019 to September 2022, an outpatient clinical study compared the efficiency of fractionated erbium:YAG laser alone (laser group) versus fractionated

#### Section A-Research paper

erbium:YAG laser with local clobetasol propionate (combined treatment group). The trial included thirty patients from aged 10-75 who met all eligibility criteria and completed all therapy sessions. The patients were recruited from the National Institute of Laser Enhanced Sciences (NILES), and Cairo Hospital of dermatology. A written consent was received from each participant describing the details of the study. An ethical consent of the project was Approved by the research and ethics committee of the NILES institute.

#### Inclusion and exclusion criteria of the study:

Subjects at least ten years of age with at least two lesions or one lesion of more than 7cm were recruiuted. Subjects should have not used or stopped using systemic or local steroids 3 months before onset of study. Patients having alopecia totalis, alopecia universalis or systemic autoimmune disorders were excluded as well as those bleeding tendency or on (anticoagulants or/and NSAID drugs). Pregnant and lactating women and those with photosensitive disorders were not included.

## **Treatment methods**

The two different treatments were given to the alopecia areata lesions at random. A simple randomization strategy was used to ensure randomization. For every patient, the lesions were classified into A and B groups (with similar SALT scores). Lesions of **group A** were treated with fractionated Er:YAG laser alone, whereas in **group B** with fractionated Er:YAG laser followed by one application of local corticosteroid cream (clobetasol propionate) immediately following the session. Laser treatments were scheduled 2 weeks apart till complete cure or for a maximum of three months. Thirty minutes just before laser treatment, a local anaesthetic cream was applied and 2 passes of fractionated Er:YAG laser (XS dynamics Fotona S1-121d, Ljubljana, Slovenia) were utilized with the following parameters: 2940 nm wavelength, with energy 3J/cm2, short pulse mode (SP), (3-5 Hz) as frequency, and spot size 7mm. Group A 5364

#### Section A-Research paper

received the laser treatment only while in group B, laser was followed by application of clobetasol propionate cream.

#### **Evaluation of Results**

The Galaxy S7 camera, which has a 12-megapixel (40323024) camera with "Dual Pixel" image sensor technology for faster autofocus and an f/1.7 aperture lens, was used to take pictures of lesions at baseline, as well as before and after sessions.

Two dermatologists blindly determined the clinical degree of AA based on the severity of alopecia SALT score, which was calculated by dividing the scalp into four quadrants and visually determining the percentage of scalp hair loss in each quadrant, then adding the numbers together for a maximum score of 100 percent.<sup>8</sup> The amount of change in SALT from baseline was determined by terminal hair growth and classified into a score: (A0) indicates no difference or further hair fall, (A1) indicates 1-24 percent hair regrowth, (A2) indicates 25-49 percent hair regrowth, and (A3) indicates 50-74 percent hair regrowth. While (A4) indicates 75-99 percent regrowth and (A5) indicate complete hair regrowth.

Dermoscopic imaging with contact dermoscopy was carried out with the aid of polarized-light (Derma Lite DL4, fourth Generation, United States of America) and a ten fold magnification. Photos were taken using a 1.5-fold optical zoom at the beginning of the procedure and then every 4 weeks. Photos were saved to pc for follow-up of activity and hair regrowth. The satisfaction of the patients was assessed on a scale of 0 till 10, where zero and ten reflect complete in satisfaction and satisfaction, respectively.

### **Statistical Analysis**

The information was gathered, coded, reviewed, and entered into IBM SPSS version 20. The qualitative data were given as numbers and percentages, the quantitative data with parametric

#### Section A-Research paper

distribution as mean, standard deviations, and ranges, and the quantitative data with nonparametric distribution as median with inter quartile range (IQR). The Kruskall Wallis test was used to compare the two groups using quantitative data and nonparametric distribution. The confidence interval was set at 95%, while the acceptable margin of error was set at 5%. As a result, a p-value of 0.05 was declared significant. In present study three months following the final laser session were the follow up period. Complications and side effects were documented.

### Results

Thirty patients, eleven women (36.7 percent) and nineteen men (63.3 percent), with age ranging of 10 to 47 years and an average 29, were included in the study. Six patients (20%) had positive family history. In 16 patients, the past medical history was positive (53 percent). The duration was ranging from two to seven months with average 3.37 m, while alopecia areata past history was ranging from 1 to 10 years with an average 2.81 years. Occipital area [nine patients (30 %)] was the most frequently affected site in the study, temporal area [eight patients (26.7 %)], parietal area [five patients (16.7 %)], then vertex [five patients (16.7 %)]. Frontal region was the least involved region [three patients (10 %)]. The median SALT score, prior to actual therapy in group A, was nine (ranging from1-18) whereas in group B was eight (ranging from 2-18). There was no statistically significant difference between the two groups (P= 0.35).

There was a statistically significant difference in clinical response between the two groups (P-value 0.032). Out of the thirty patients of **group A**, three patients (10 %) had a complete response (A5), 22 patients (73.33 %) had a partial response [1 patient (3.3 %) had a scoring rate A1, 2 patients (6..7 %) had a scoring rate A2, 6 patients (20 %) had a scoring rate A3, and 13 patients (43.3 %) had a scoring rate A4], and 5 patients (16..7 %) had zero reaction (A0). In **group B**, eleven patients (36.7 %) out of the thirty had a complete response (A5), seventeen (56.6 %) had a moderate improvement, one patient (3.3 %) had a scoring rate A1, one patient

Section A-Research paper

(3.3 %) had a scoring rate A2, three patients (10 %) had a scoring rate A3, and twelve patients (40%) had a scoring rate A4 and two patients (6.7 %) had zero reaction (A0). Table 1

Both groups demonstrated a significant SALT score reduction (p < 0.001) with group B showing a more significant reduction when compared to group A (p = 0.032) (Figs. 1- 3 and Tab. 1). The duration of AA did not significantly impact the response of treatment in both groups.

Once the dermoscopic results in the **group** (**A**) were compared before and after laser therapy, there was a major drop in yellow dots (from 76.7 percent to 33.3 percent), exclamation marks (from 63.3 percent to 16.7 percent), black dots (from 50 percent to 13.3 percent), empty follicles (from 30 percent to 6.7 percent), and a significant increase in short vellus hairs (from 20 percent to 50 percent, p=0.001). In **group** (**B**) a reduction in yellow dots was demonstrated after treatment (from 76.7 percent to 23.3 percent), exclamation mark hairs decreased (from 63.3 percent to 10%), black dots (from 50 percent to 10 percent), empty follicles (from 30 percent to 6.7 percent), and a significant increase in short vellus hairs decreased (from 63.3 percent to 10%), black dots (from 50 percent to 10 percent), empty follicles (from 20 percent to 53.3 percent), and a significant increase in short vellus hair was reported (from 20 percent to 53.3 percent, p=0.01). Figs 2,4; Tables 2-4 There was no significant superiority in dermoscopic assessment to one group over the other following treatment. Patient satisfaction questioned on a 10 point scale demonstrated non significant superiority or satisfaction with one treatment over the other at the end of the study. Table 5

#### Discussion

Alopecia Areata (AA) is an autoimmune mediated disorder. It is characterized as non-scarring inflammatory hair fall with a negative impact on patients' life quality.<sup>9</sup> Topical and Intralesional corticosteroids (ILC) are the first-line treatments for limited AA.<sup>10</sup> In adults with patchy disease, ILC is preferred over topical steroids for their faster, longer action, and deeper penetration. However, ILCs are associated with intolerable pain. Laser-assisted drug delivery 5367

#### Section A-Research paper

(LAD) overcomes this obstacle and allows uniform, deeper penetration of topical agents with much less pain.<sup>11</sup> The goal of this study was to compare two lines of treatment of AA [fractionated Er:YAG laser alone (**group A**) versus fractionated Er:YAG laser combined with local clobetasol propionate (**group B**)]. Following treatment both groups experienced a significant reduction in SALT score; more significantly noted in group B (P value was 0.032). The reported results agreed to what Yoo et al. demonstrated by complete resolution of hair loss in alopecia of a 35 yes old male after six sessions of fractional laser treatment.<sup>12</sup>

Cho et al. investigated the therapeutic efficacy of combining an Erbium glass with fractionated CO2 lasers on 3 patients having alopecia areata. According to a blinded investigator's physician global assessment, two patients improved greatly, whereas the third did not.<sup>13</sup>This is in line with the findings of Majid et al., who performed 8 fractionated co2 laser treatments combined with topical steroid application in ten cases of refractory alopecia areata and demonstrated a significant recovery in nine of the treated cases.<sup>14</sup>

The efficacy of a 1540-nm fractional erbium-glass laser on AA was investigated in a recent case-control study. Thirty individuals with 60 AA patches were treated with six sessions of fractional erbium-glass laser treatment with topical minoxidil at one-week intervals, while the control patches just received topical minoxidil. After 6 weeks, the response rate in the control group was 16 percent, whereas in the study group it was 60 percent, demonstrating that the erbium-glass laser improved significantly the impact of topical minoxidil.<sup>15</sup>

These results agreed with El Husseiny et al., who described a significant improvement in the patches treated with FCL, with 60% of their patients showed >75% improvement.<sup>16</sup> Our results were compatible to those by Nouh and colleagues who reported a significant hair regrowth in 40 patients complaining of AA following fractional laser treatment.<sup>17</sup>

Contrary to our findings, in a prospective controlled trial involving 32 patients with refractory 5368

#### Section A-Research paper

AA, Yalici-Armagan and Elcin investigated ablative fractional  $CO_2$  laser as a monotherapy resulting in insignificant increase in mean hair count when compared to control areas.<sup>17</sup> This difference could be explained by the fact they included refractory cases with long disease duration of more than 12 months.

Meanwhile, fractional lasers promote hair regrowth by causing T cell apoptosis, peribulbar lymphocyte dispersion, increasing blood flow promoting and telogen to anagen transitions. There is reported synergism of fractionated laser and local steroid that could be explained by direct therapeutic effect of fractionated laser combined with transepidermal delivery (TED) into the target hair follicles.<sup>19</sup> Both processes may be engaged in alopecia areata hair growth promotion.<sup>14</sup> Application of laser is also less painful with fewer side effects compared to intradermal injections especially in children.

In agreement with us, Soror et al., and Abdel Meguid et al., reported significant improvement in grading AA patches treated by fractional laser plus triamicinolone.<sup>20-21</sup> A recent study by Tanakol et al., involving 25 Turkish patients complaining of chronic AA patients, found that 62.5% of patients with patchy AA of the scalp had at least 50% improvement in SALT score, while patients with alopecia universalis were all non responders except for one patient with minimal response.<sup>22</sup> The less chronivcity of cases in our study and the more number of sessions and different laser parameters used by us compared to Tanakol et al.<sup>22</sup> ( 6 vs.3) could explain our more favorable response

The most common noticed dermoscopic features in this study was yellow dots, black dots, broken hair, exclamation mark hair and short vellus hairs in agreement with others.<sup>11, 23</sup> both groups showed post-treatment decline in YD, BD, BH, EMH, parallel with significant increase of short vellus hair. This was in agreement with reports from previous studies.<sup>20, 24, 25</sup>

Section A-Research paper

All patients developed transient post treatment erythema and mild scaling. mild to moderate pain occurred during laser sessions, and the mean Numerical rating scale (NRS) for pain was  $1.2 \pm 0.7$ . There were no signs of subsequent infections, bullae development, post inflammatory pigmentations, or scar tissue formation after treatment. No recurrence was recorded in the subsequent three months. Limitation of the study included the small sample size, a non-controlled trial, and the short follow-up period.

In conclusion we shed light and reported the dual significant effect played by fractional laser directly and more significantly through laser assisted delivery of clobetasol proprionate. in treating AA. Better results might be expected with early treatment and longer treatment durations. Larger studies are needed to confirm the efficacy of fractional Er:YAG laser and define appropriate treatment parameters and treatment protocols.

Section A-Research paper

## **Table legends**

- Table (1) Percentage of scalp hair regrowth based on SALT score
- Table (2) Dermoscopic signs before treatment
- Table (3) Comparison between dermoscopic signs before and after laser treatment
- **Table (4):** Comparison between dermoscopic sings before and after combined both therapy.

 Table (5): Compaction between Patients satisfaction in laser and combined both treatment

## **Figure Legends**

**Figure (1)** A 25-year-old female patient presented by two AA. The blue square represents the lesion treated solely with fractional laser (A3), while the green square represents the lesion treated with laser and steroid (A5). [A: prior to treatment, B: six sessions later]

**Figure (2)** Dermoscopy of a lesion treated with a fractional laser only [before and after treatment (A,B)], dermoscopy of a lesion treated with a fractional laser followed by a topical steroid [before and after treatment (C,D)] showing decreased yellow dots, black dots, exclamation mark hair, broken hairs and increased vellus hair..

**Figure (3)** A 23-year-old male presented by multiple AA. The blue square represents the lesion treated solely with fractional steroid (A4), while the green square represents the lesion treated with laser followed by topical steroid A5 [A: prior to treatment, B: 6 sessions later].

**Figure (4)** Dermoscopy of a lesion treated with a fractional laser only [before and after treatment (A,B)], dermoscopy of a lesion treated with a fractional laser followed by a topical steroid [before and after treatment (C,D)] showing decreased yellow dots, black dots, exclamation mark hair, broken hairs and increased vellus hair..

5371

Section A-Research paper

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Section A-Research paper

	lase	La laser group		aser-steroid group	
	No	percentag e	No	percentage	
A0*	5	16.7%	2	6.7%	
A1	1	3.3%	1	3.3%	
A2	2	6.7%	1	3.3%	
A3	6	20%	3	10.0%	
A4	13	43.3%	12	40.0%	
A5	3	10%	11	36.7%	
Laser-steroid vs. fractional laser alone (p value)	*0.032				

Table (1): Percentage of scalp hair regrowth based on SALT score

\* (A0) indicates no difference or further hair fall, (A1) indicates 1-24 percent hair regrowth, (A2) indicates 25-49 percent hair regrowth, and (A3) indicates 50-74 percent hair regrowth. While (A4) indicates 75-99 percent regrowth and (A5) indicate complete hair regrowth. Categorical data expressed as Number (%) \*: Statistically significant (P<0.05) ; The Severity of Alopecia Tool (SALT)

Section A-Research paper

Dermoscopic sings	Before		
	No.	%	
Yellow dots	23	76.7%	
Exclamation marks	19	63.3%	
Black dots	15	50.0%	
Empty follicles	9	30.0%	
White dots	12	40.0%	
Broken hairs	13	43.3%	
Short vellus hair	6	20.0%	

# Table (2) Dermoscopic signs before treatment

Categorical data expressed as Number (%)

Section A-Research paper

Dermoscopic signs	Before Laser		After L	aser	Chi square test	
	No	%	No	%	X <sup>2</sup>	P value
Yellow dots	23	25.0%	10	23.8%	0.022	0.882
Exclamation marks	19	20.7%	5	11.9%	1.501	0.220
Black dots	15	16.3%	4	9.5%	1.089	0.296
Empty follicles	9	9.8%	2	4.8%	0.965	0.325
White dots	7	7.6%	3	7.1%	0.009	0.924
Broken hairs	13	14.1%	3	7.1%	1.339	0.247
Short vellus hair	6	6.5%	15	35.7%	18.595	* 0.001

Categorical data expressed as Number (%)  $\chi$ 2: Chi-square test \*: Statistically significant (P< 0.05)

 Table (4) Comparison between dermoscopic sings before and after combined both therapy.

Dermoscopic signs		Before combined therapy		fter combined therapy	Chi square test	
	No	%	No	%	X <sup>2</sup>	P value
Yellow dots	23	25.0%	7	19.4%	0.445	0.504
Exclamation marks	19	20.7%	3	8.3%	2.759	0.096
Black dots	15	16.3%	3	8.3%	1.360	0.243
Empty follicles	9	9.8%	2	5.6%	0.589	0.442
White dots	7	7.6%	2	5.6%	0.167	0.682
Broken hairs	13	14.1%	3	8.3%	0.795	0.372
Short vellus hair	6	6.5%	16	44.4%	26.144	* 0.001

Categorical data expressed as Number (%)  $\chi$ 2: Chi-square test \*: Statistically significant (P< 0.05)

Section A-Research paper

 Table (5) Compaction between Patients satisfaction in laser and combined both treatment

Patients		Laser	aser Combined treatment		P value	
satisfaction	NO	%	NO	%		
0	0	0.0%	1	3.3%	NA	
1	5	16.7%	4	13.3%	0.717	
2	1	3.3%	1	3.3%	1.00	
3	1	3.3%	3	10.0%	0.30	
4	0	0.0%	3	10.0%	NA	
5	2	6.7%	2	6.7%	1.00	
6	2	6.7%	3	10.0%	0.64	
7	4	13.3%	3	10.0%	0.68	
8	7	23.3%	3	10.0%	0.165	
9	7	23.3%	6	20.0%	0.75	
10	1	3.3%	1	3.3%	1.00	

Categorical data expressed as Number (%) \*: Statistically significant (P< 0.05)

Section A-Research paper



Figure 1: A 25-year-old female patient presented by two AA. The blue square represents the lesion treated solely with fractional laser (A3), while the green square represents the lesion treated with laser and steroid (A5). [A: prior to treatment, B: six sessions later]

Section A-Research paper



Figure 2: Dermoscopy of a lesion treated with a fractional laser only [before and after treatment (A,B)], dermoscopy of a lesion treated with a fractional laser followed by a topical steroid [before and after treatment (C,D)] showing decreased yellow dots, black dots, exclamation mark hair, broken hairs and increased vellus hair.

Section A-Research paper



Figure 3: A 23-year-old male presented by multiple AA. The blue square represents the lesion treated solely with fractional steroid (A4), while the green square represents the lesion treated with laser followed by topical steroid A5 [A: prior to treatment, B: 6 sessions later].

Section A-Research paper



Figure 4: Dermoscopy of a lesion treated with a fractional laser only [before and after treatment (A,B)], dermoscopy of a lesion treated with a fractional laser followed by a topical steroid [before and after treatment (C,D)] showing decreased yellow dots, black dots, exclamation mark hair, broken hairs and increased vellus hair.