



Comparative Study between Ablative Fractional Carbon Dioxide Laser Combined with Topical Steroid Versus Topical Steroid in Treatment of Alopecia Areata

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ABSTRACT:

BACKGROUND:

Alopecia areata is a prevalent disorder that impacts the mental health of those who suffer from it. When it comes to managing it, no one therapy approach has been proven to be both effective and safe. Various dermatological illnesses can now be managed with the use of laser-assisted drug delivery. One possible mechanism of action for fractional laser therapy is to promote telogen to anagen transitions, increase blood flow, and induce T cell death. Hair can be stimulated to grow after minor damage or wound healing.

OBJECTIVE:

To assess the efficacy of topical steroid administration aided by fractional carbon dioxide lasers in the treatment of alopecia areata.

PATIENTS AND METHODS:

A total of 20 patients with (108 patches) of alopecia areata with two or more nonadjacent patches are included. After complete medical history and physical examination, all patients were given clobetasol propionate 0.05% cream twice daily on all patches then the patches on the same patient are categorized into two groups, group A treated with fractional carbon dioxide laser in addition to clobetasol propionate 0.05% cream and the group B treated with clobetasol propionate 0.05% cream alone. Assessment was done by MacDonald Hull and Norris grading. A total of four sessions were done at 2 week interval (baseline, 2nd week visit, 4th week visit, 6th week visit) then patients were seen after 2 weeks from last session (8th week) for assessment and seen after two month from the last session for follow up.

RESULTS:

There is significant statistical difference observed between both groups. Group A had better treatment outcome as compared to Group B during all treatment intervals. Regarding duration comparison during treatment period from 2 to 8 weeks, a significant result obtained (P=0.000) regarding Group A but Group B showed non-significant difference (P=0.112). Furthermore, duration comparison during follow-up period from the last session to two months, showed a significant result obtained regarding Group A (P=0.000) and Group B revealing non-significant difference (P=0.059). Finally, at two month follow up Group A was found to be significantly different from Group B.

CONCLUSION:

The results show that the combination of fractional CO₂ laser and clobetasole propionate 0.05% cream effectively treats localized alopecia areata. It outperformed monotherapy with clobetasole propionate 0.05% cream.

KEY WORDS: Alopecia areata, Fractional co₂ laser , Clobetasole propionate .

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INTRODUCTION:

Alopecia areata (AA) is an autoimmune disease of the hair follicles. It is characterized by a well-defined non-scarring alopecic patch or patches that may extend to the entire scalp or lead to total body

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hair loss⁽¹⁾. The presence of lymphocytic infiltrations surrounding the hair follicles and IFN- γ are the reasons behind hair loss in alopecia areata. In addition, people with alopecia areata often have IgG antibodies that target the cells of the hair follicle. Furthermore, infections or inflammation can trigger the condition, and it often occurs alongside other autoimmune disorders.⁽²⁾

Alopecia areata can go through a variety of surprising phases, including spontaneous remission. Relapses, significant hair loss, and protracted periods without regrowth are all symptoms that some patients may face.⁽³⁾ Due to its modest side-effect profile when used with caution, topical corticosteroids are commonly prescribed to children and used to treat localized patchy AA. Additionally, for more severe cases, they are suggested as an additional course of treatment. There is a wide variety of topical galenic formulations of corticosteroids available presently, including shampoos, solutions, and foam preparations⁽⁴⁾

The use of lasers as an additional therapeutic option for AA started relatively recently, when the term "paradoxical hypertrichosis" was first coined to describe the unusual growth of hair in patients who had intensive pulsed light therapy for photoepilation⁽⁵⁾.

There has been a steady uptick in research into the usage of lasers to treat AA, although the precise processes by which these treatments work remain unclear. A number of laser treatments have demonstrated therapeutic success; thus, they have been proposed as an additional alternative for the treatment of refractory AA, however they are not commonly employed in comparison to other treatment methods⁽⁶⁾.

The term "transdermal drug delivery" refers to a system that uses physical means to help move drugs over the skin's surface. This exciting new way of administering drugs to the body allows for better absorption than is feasible with topical administration. Lasers, dermabrasion, microneedling, pressure waves, and the vacuum effect have all been studied in relation to transdermal drug administration⁽⁷⁾.

A novel therapeutic approach called ablative fractional resurfacing (AFR) produces tiny vertical holes in the skin that are ablated and then encircled by a thin layer of coagulated tissue; these holes are called microscopic treatment zones (MTZ). Although AFR only affects a small section of skin,

there are tiny gaps in the skin's surface that allow for scar-free regeneration. Photodamaged face skin, rhytides, acne scars, and burn scars are among of the conditions that have been treated using the AFR approach for dermal remodeling. Since the ablated laser holes extend into dermis, they may theoretically serve as conduits for drug absorption, which means that AFR may also help in the penetration and distribution of topically applied pharmaceuticals.⁽⁸⁾

AIM OF THE STUDY:

To evaluate the efficacy of fractional carbon dioxide laser in combination with clobetasol propionate 0.05% cream in the treatment of alopecia areata compared with clobetasol propionate 0.05% cream alone.

PATIENTS AND METHODS:

Taking place from August 2021 to September 2022, this interventional comparative treatment study was carried out at the center of dermatology in Medical City, Baghdad, Iraq. This research comprised twenty participants who had 108 alopecia areata patches.

Inclusion Criteria

1. Patient Age > 6 years old.
2. Patients with at least two patches or more of alopecia areata of at least 1 year duration.
3. Not responding to two or more different lines of treatment.
4. Patients who didn't receive any type of alopecia areata treatment modality for at least the past two months.

Exclusion Criteria

1. Pregnant ladies and lactating mothers.
2. History of keloid or hypertrophic scar.
3. Active herpetic infection.
4. History of contagious diseases.
5. Mentally retarded individuals.

Ethical Consideration

1. Before being included in the trial, each patient was asked to provide written informed permission.
2. The procedure, its modalities, and potential problems were thoroughly explained to the patients.
3. This study was approved by scientific committee of Iraqi Board of Dermatology and venereology - Iraqi board for medical specialization.

The diagnosis of alopecia areata was done clinically. Full history was taken from patients. Physical examination was done for each patient for

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number, site, and size of the patches and the presence of exclamation mark hair. Nails were also examined for any associated changes. All patients in the study were instructed to apply clobetasol propionate cream on the patches twice daily with gentle massage for 3-5 minutes for 8 weeks., then at least 2 patches were selected randomly to be treated as group A or B fifty-four patches for each. The patches in both groups were duration matched.

Group A; fractional CO₂ laser in combination with clobetasol propionate cream:

Prior to each treatment session, the area was cleansed with non-abrasive detergent and gauzes soaked in normal saline after one hour of application of topical anesthesia. Laser parameter was adjusted as (power dwell time dot spacing fluence) then clobetasol propionate applied within 30 minutes for the patch that selected as group A.

Group B; Clobetasol propionate 0.05%cream alone:

were treated with clobetasol propionate 0.05% cream alone.

A total of four sessions were done at 2 week interval (baseline, 2nd week visit, 4th week visit, 6th week visit) then patients were seen after 2 weeks from last session (8th week) for assessment and seen after two months from the last session for follow up.

Assessment was done by MacDonald Hull and Norris grading. G0: No hair regrowth.

G1a: Partial vellus hair regrowth (fine, short and lightly pigmented hair).

G1b: Partial terminal hair regrowth (coarse, darkly pigmented hair).

G2: Complete terminal hair regrowth.

Patients' degree of satisfaction was scored using subjective patients' satisfaction, for each patch as follow: 0=Unsatisfied, 1=Slightly Satisfied, 2=Satisfied, 3=Very satisfied

RESULTS:

The participants were followed up and assessed at 2 weeks, 4 weeks, 6 weeks, 8 weeks and after two months for follow up.

Within 2 months, significant difference observed between Group A and Group B (P=0.000) regarding final follow-up treatment outcome.

Regarding duration comparison during treatment period from 2 to 8 weeks, a significant result obtained (P=0.000) regarding Group A but Group B showed non-significant difference (P=0.112).

Furthermore, duration comparison during follow-up period from the last visit to 2 months, a significant result obtained (P=0.000) regarding Group A and Group B revealed non-significant difference (P=0.059).

All these results were illustrated in Table (1) , (2), and Figure (1) .

Table 1: The response of the patches to therapy in Group A,B in each visit.

Variable	Group A		Group B		P value
	Laser+Steroid		Steroid only		
	N	%	N	%	
2nd week visit					
no hair regrowth	37	68.5	52	96.3	0.000*
partial vellus hair regrowth	17	31.5	2	3.7	
partial terminal hair regrowth	0	0	0	0	
Complete terminal hair regrowth	0	0	0	0	
4th week					
no hair regrowth	21	38.9	51	94.4	0.000*
partial vellus hair regrowth	25	46.3	3	5.6	
partial terminal hair regrowth	8	14.8	0	0	
Complete terminal hair regrowth	0	0	0	0	
6th week					
no hair regrowth	8	14.8	50	92.6	0.000*

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partial vellus hair regrowth	27	50	3	7.4	
partial terminal hair regrowth	19	35.2	1	0	
Complete terminal hair regrowth	0	0	0	0	
8th week					
no hair regrowth	5	9.3	49	90.7	0.000*
partial vellus hair regrowth	12	22.2	4	9.3	
partial terminal hair regrowth	28	51.9	1	0	
Complete terminal hair regrowth	9	16.7	0	0	
Duration comparison					
			P=0.000*	P=0.112	

Table 2: Comparison of the studied groups at (16 weeks) two months follows up.

Variable	Group A		Group B		P value
	Laser+Steroid		Steroid only		
	N	%	N	%	
Two months					
no hair regrowth	5	9.3	45	83.3	0.000*
partial vellus hair regrowth	6	11.1	8	14.8	
partial terminal hair regrowth	14	25.9	1	1.9	
Complete terminal hair regrowth	29	53.7	0	0	
Duration comparison (8 weeks-16 weeks)					
			P=0.000*	P=0.059	

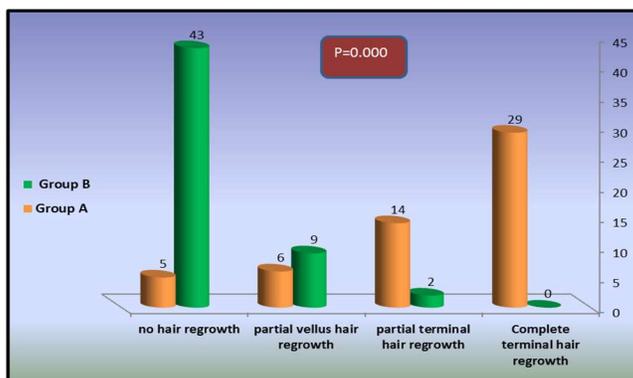


Figure 1: Comparison of the studied groups at the end of the study period (two months).

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Figure 2: A 6 years old female with patchy alopecia areata of 2 years duration with poor response to intralesional steroid and excimer laser (A) group A before ; (B) group A after ; (C) group B before and (D) group B after treatment.



Figure 4: A 9 years old male with patchy alopecia areata of 1 year duration with poor response to topical and systemic steroid (A) group A before ; (B) group A after ; (C) group B before and (D) group B after treatment.

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Figure 5: A 42 years old female with patchy alopecia areata of 4 years duration with poor response to intralesional and systemic steroid and topical minoxidil. (A) group A before ; (B) group A after ; (C) group B before and (D) group B after treatment.

DISCUSSION:

Hair loss can range from a few tiny patches to total baldness due to a chronic inflammatory non-scarring disorder called alopecia areata. Despite the abundance of therapy options, no one approach has demonstrated consistent efficacy in the management of AA⁽⁹⁾.

Ablative fractional laser therapy is one of the most innovative and safest options for alopecia areata. One possible mechanism of action for fractional laser therapy is to promote telogen to anagen transitions, increase blood flow, and induce T cell death. A person's hair may begin to grow back after a little injury or wound heals⁽⁹⁾.

A research using a mouse model demonstrated that fractional CO₂ laser therapy led to anagen induction via the Wnt/ β -catenin pathway, which in turn caused hair regrowth and an increase in the proportion of anagen hairs. It was also shown that there was an upregulation of Wnt10-b and an increase in the mRNA expression of many growth

factors linked to wound healing, such as vascular endothelial growth factor (VEGF), transforming growth factor β 1 (TGF- β 1), and keratinocyte growth factor (KGF)⁽⁹⁾.

In 82% to 86% of instances, AA begins before the age of 40, and most research on the subject have failed to find a substantial difference in incidence between males and females, according to a retrospective study series by Harries et al., which is consistent with the results of this investigation⁽¹⁰⁾. Roughness pitting complete nail dystrophy was the diagnosis for 25% of the cases of nail alterations. These are a typical AA symptom. This is in line with the findings of Chelidze and Lipner, who postulated that AA is associated with a 30% average prevalence of nail changes, which can lead to substantial deformity and functional loss. The two most common manifestations of AA, pitting and trachyonychia, were found to be 8% and 20% of the cases, respectively⁽¹¹⁾.

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According to Harries et al., who found that a number of autoimmune conditions may be more common in people with AA than in the general population, 15% of participants had a history of systemic diseases, suggesting that AA could occur in conjunction with other autoimmune diseases⁽¹⁰⁾. A meta-analysis of 17 studies found that the frequency of thyroid disease was much higher in AA patients compared to controls. Based on these findings, screening for thyroid dysfunction should be considered for AA patients⁽¹²⁾.

The results showed that the group treated with a combination of CO₂ laser and topical steroids had significantly better outcomes than the group treated with steroids alone, particularly at 2, 4, 6, and 8 weeks, according to the MacDonald Hull and Norris grading system.

These findings corroborate those of Majid et al., who demonstrated that a combination of fractional CO₂ laser and triamcinolone solution may be a successful alternative for resistant alopecia areata⁽¹³⁾.

In a separate trial, Abdel Halim et al. found that the FRCO₂ laser, either alone or in conjunction with betamethasone valerate cream, had a substantial impact⁽⁹⁾.

Since the hair follicle is located in the dermis and subcutaneous fat, below the stratum corneum, it might be difficult to guide medicines to this specific area when treating alopecia. The stratum corneum, which is composed of keratinocytes arranged in layers within a complex matrix of ceramides, free fatty acids, and cholesterol, is around 10-15 μm thick⁽¹⁴⁾.

This creates an obstacle for the topical administration of medications, especially those that are hydrophilic or large hydrophobic molecule. A potential solution to this slowing down of medication distribution to deeper layers of skin and the cutaneous vasculature is the employment of new technology like fractional lasers and microneedling devices. In ablative fractional laser operations, the devices are used to generate vertical regions of ablated tissue called tiny treatment zones, and in microneedling, the devices are used to physically puncture the skin⁽¹⁴⁾.

Transcutaneous drug delivery for the management of alopecia areata via FCO₂, microneedling was assessed by Abdelwadoud et al which show significant improvement of both groups⁽¹⁵⁾. Salman and Alnashmy et al, conducted a comparative study between micro-needling

combined with topical steroid and topical steroid alone and founded that combination modality is superior to topical steroid alone⁽¹⁶⁾. In a research comparing intralesional steroid therapy to fractional carbon dioxide laser-assisted topical steroid administration for alopecia areata, Soror et al. found similar results⁽¹⁾. Alopecia areata therapy options include topical steroid administration assisted by fractional carbon dioxide laser, which shows promise.

The low pain score in individuals treated with laser-assisted medication delivery is more advantageous⁽¹⁷⁾, even though intralesional steroid therapy demonstrated more substantial outcomes⁽¹⁷⁾. Al-Dhalimi et al. also used a 1,540 nm Fractional Erbium- Glass laser in the treatment of AA with minoxidil in six sessions during six weeks which seem to be effective⁽¹⁸⁾.

Although Erbium glass laser is a non-ablative but still an effective in inducing a hair regrowth probably due to its thermal effect on papillary dermis, or an immunological effect on hair follicle and may enhancing the delivery of minoxidil solution.

Regarding observer assessment of degree of improvement showing a higher degree of improvement in group A which support our results. Patients satisfaction scale results also in line with our study as 70% of patients in group A satisfied to very satisfied which is our goal to improve patients wellbeing socially as alopecia areata is debilitating depressing stigmatizing disease.

CONCLUSION:

When used with clobetasole propionate 0.05% cream, the FRCO₂ laser is a viable therapy option for localized AA. It was proven to be more effective than clobetasol propionate 0.05% cream monotherapy.

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