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Original article

Efficacy of Intralesional Vitamin D in the Treatment of Alopecia Areata Using Dermoscopy before and after Treatment

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ABSTRACT

Background: Alopecia Areata (AA) is an autoimmune disease that targets hair follicles and is driven by T cells specific to that organ. As it was found that the lack of expression of VDRs is associated with reduced hair follicle growth and epidermal differentiation. The aim of this study was to evaluate the efficacy and safety of intralesional vitamin D and to assess it by the dermoscope. **Methods:** This study is A clinical trial study that included 20 patients with alopecia areata, who received intralesional injection of vitamin D (an aqueous preparation of cholecalciferol (Devarol ampule 200000iu/2ml, Memphis, Egypt) (2.5mg/ml) the maximum total amount of Vitamin D3 injected in every session was 1.25mg (0.5ml).Treatment of alopecia areata was done according to the study protocol and the patients were evaluated at initial Visit, every 2 weeks during treatment sessions and 3 months after completion of therapy. **Results:** There was no statistical significance change in SALT score among our group patients post treatment compared to pretreatment, regarding clinical response there was 10% of cases (2 patients) shows hair regrowth by >25% (A2) and majority of patients 75% (15 patients) shows minimal hair regrowth by < 25% (A1), 15% of cases (3 patients) showed no improvement at all , there was erythema, itching and pain assessed among study cases (20%, 15% and 15% respectively). Atrophy and telangiectasia were found among 5% in cases.**Conclusions:** Intralesional Vitamin D (cholecalciferol) is a mild effective treatment of Alopecia Areata.
Keywords: Alopecia Areata; VitaminD**;** Dermoscopy.

INTRODUCTION

Alopecia Areata (AA) is a common, nonscarring autoimmune skin disorder that affects about 2% of the general population. Clinical symptoms can range from a slight loss of hair to the full absence of hair on the body and scalp **[1]**.

For many patients, spontaneous remission happens. About half of those with mild patchy hair loss may fully recover in a year, however nearly all will go through multiple episodes of the illness. Alopecia Areata, however, can linger for several years, and in certain instances, hair growth never fully recovers. Alopecia totalis or alopecia universalis affects about 10% of patients **[2].**

Most patients are generally youthful, and the disease burden is ordinarily considerable, prompting overpowering consequences for the patient's personal satisfaction and self-esteem. Treatment is still a challenge in Alopecia Areata, and there is numerous remedial modalities to treat it with variable viability and security profile **[3]**.

Topical immunotherapy, minoxidil, anthralin, corticosteroid injections, corticosteroid creams, and phototherapy are among the treatment options for AA. The patient's age (young children may not always tolerate side effects), the severity of their ailment (localized vs. extensive), and their preferences

will all influence which agent is best for them **[4]**.

It has been shown that the keratinocytes seen in hair follicles from mice and humans prominently express 1,25-dihydroxyvitamin D (3) receptors (VDRs), and that the absence of VDR expression is linked to decreased epidermal differentiation and hair follicle growth **[5].** Recent research findings indicate that patchy AA of the scalp may benefit from topical use of calcipotriol, a vitamin D3 equivalent **[6].**

This study was conducted to evaluate the efficacy and safety of intralesional vitamin D and to assess it by the dermoscope.

METHODS

This study clinical trial was conducted at Zagazig university Hospitals in the out-patient clinic of Dermatology, Venereology and Andrology Department, during the period from February 2022 till December 2022. Written consent was taken from each patient before involvement in the study.

This study was approved by Zagazig University Institutional Review Board (IRB# 9109-21-11-2021).

This study included healthy Patients of both sexes having typical clinical findings (round oval patches of non-scarring hair loss) that confirmed by dermoscopic examination (yellow dots, exclamation mark and black dots) of different duration and activity, both sexes were included, at any age group.

Exclusion criteria included patients with a systemic disease as hypothyroidism, diabetes, damage of the liver, kidneys, or other autoimmune conditions like systemic lupus erythematosus, patients with other dermatological disease such as psoriasis and vitiligo, patients on topical treatment during the last month before study, patients on systemic treatment (corticosteroid, cyclosporine A, phototherapy) two months before the study, pregnancy and lactation and any known sign of active infection or inflammation at the site of treatment or allergy to the used treatment.

Twenty patients with localized patchy Alopecia Areata were included in our trial. Every case had a thorough history taking, clinical, and dermoscopic assessment.

Complete general and dermatological examinations including the nails were done to exclude the presence of any correlating systemic and /or dermatological diseases. Local scalp assessment was conducted to validate the diagnosis, and to determine clinical variants and for assessment disease severity, Trichoscopic examination and photographic documentation were done. All previous data was documented and filed.

Twenty patients received intralesional injections of vitamin D3, an aqueous cholecalciferol formulation, (Devarol ampule 200000iu/2ml, Memphis, Egypt) (2.5mg/ml) A maximum of 1.25 mg (0.5 ml) of vitamin D3 could be injected during each session.

Treatment was for 3 months and all intralesional treatments were applied to the affected areas every two weeks at regular follow up visits for 6 sessions of treatment.

Clinical examination and digital images of the hair loss lesions was performed at start of the study, and each visit every two weeks. Dermoscopic evaluation was done to all patients before and after the study. Follow up of patients was done every month for 3 months based on clinical and dermoscopic evaluation.

Timing of assessment

Every two weeks during the treatment till completion of therapy (6 sessions). Observation of initial hair regrowth, new patches appearance and recording of side effects were done at each visit (before starting the treatment).

Severity of Alopecia Tool (SALT) score

Clinical evaluation of the patients was done before the start (week 0) and at the end of the study (week 12) by utilizing the severity of alopecia tool (SALT) score to determine the extent of clinical improvement, which was assessed according to:

SALT (Global SALT)

The disease severity was assessed at baseline and at each visit using global severity score known as the 6-point "Severity of Alopecia

Tool," or SALT score, a quantitative way of assessing scalp hair loss **[7].**
(S0 = no alopecia and S5 = alopecia totalis)

Hair regrowth assessment.

We calculate the average percentage of hair regrowth at the most recent follow-up visit using the hair regrowth (based on SALT score):

A_0 = no change or further loss, A_1 = 1-24% regrowth, A_2 = 25-49% regrowth, A_3 = 50-74% regrowth, A4 = 75-99% regrowth and A_5 = 100% regrowth **[7].**

In this study, dermoscopic examination (polarized dry contact approach) was used to detect the presence of trichoscopic specific findings of AA such as

Yellow dots: they are equivalent to filled follicular infundibula with keratinous materials and/or sebum; they indicate severity of AA **[8]**.

Black dots: these represent the remnants of broken hairs, hairs with exclamation marks or tapering hairs, which serve as a sensitive indicator of both the severity and course of the AA disease **[8,9].**

Broken hairs: they are thought to be indicators of disease activity and to be formed by dystrophic hairs **[8,10].**

Tapered hairs: they represent Hair shafts narrowing in the direction of the follicles (elongated exclamation mark hair) and can be observed on naked eye examination at perilesional area. They are thought to be a sign of illness activity **[8].**

Short vellus hairs: These are the most common during the persistent and intermittent phase of AA **[11]**. They appear as fresh, thin, and unpigmented hairs, which may or may not show up on a clinical examination. Their presence together with a sign of transformation into terminal hairs indicates good prognosis **[9].**

Terminal hairs: increased pigmentation and thickness of the proximal shaft of hair indicating good response to treatment **[12, 13].**

The time of initial response was noticed via dermoscopy during follow up sessions. Pigtail hairs or pigmented, upright regrowing hairs were early indicators of hair regrowth and indicated the initial reaction.

STATISTCAL ANALYSIS

SPSS version 25 was used for data processing; data were verified, input, and examined. For qualitative variables, the information was presented as a percentage and a number, and for the quantitative variables, as mean + standard deviation (SD). Mc-Nemar test was used to calculate serial change over time. The I-Krusskal-Walis test was utilized in several groups to compute the difference between quantitative variables in data that was not regularly distributed. Chi-square test (X^2). The level statistical significance was set at 5% level (P-value)

RESULTS

Table 1; showed that age of our group patients ranges from 7 to 41 years, 25% of our patients were females and 75% males, disease duration ranges from 1 to 32 months, there was negative family history, and no previous treatment was taken by patients before our study.

Table 2; showed that there were no statistical significance differences in SALT score pretreatment and post treatment.

Table 3; showed that no nail abnormalities were found among our patients.

Table 4; regarding adverse effects of treatment,there was erythema, itching and pain assessed among study cases (20%, 15% and 15% respectively). Atrophy and telangiectasia were found among 5% of cases.

Table 5; showed that 10% of cases (2 patients) shows hair regrowth by >25% (A2) majority of our patients (75%) shows mild hair regrowth <25% (A1), and 15% of cases with no response (A0).

Table (1): Demographic data of the study group: Q

Variable		**(IL vit.D) (*n*=20)**	
Age: (years)	Mean ± SD Median Range	23.5 ± 11.4 27 7 - 41	
Variable		**No**	**%**
Sex:	Female Male	5 15	25 75
Disease duration (months)	Mean ±SD Median Range	12.2 ± 11.39 1-32	
Family history:	-ve +ve	20 0	100 0
Previous treatment:	No Yes	20 0	100 0

SD: Stander deviation, **KW:** Kruskal Wallis test,
χ^2**:** Chai square test.

ble (2):SALT score pre & post treatment:

Variable		**(IL vit. D) (*n*=20)**	
		No	**%**
Score before:	**1** **2** **4**	18 2 0	85 15 0.0
Score After:	**0** **1** **4**	0 20 0	0.0 100 0.0
P^		**0.891**	
% of change		**10%**	

χ^2**:** Chai square test. **P^:** McNemar test

Table (3): Nail abnormalities:

Variable		**(IL vit. D) (*n*=20)**	
		No	**%**
Nail abnormality:	No Yes	20 0	100 0

χ^2**:** Chai square test. **S:** significant (P<0.05)

Table (4): Adverse effects of treatment:

Variable		(IL vit. D) (*n*=20)	
		No	**%**
Erythema:	Yes	4	20
	No	16	80
Itching	Yes	3	15
	No	17	85
Pain	Yes	3	15
	No	17	85
Atrophy	Yes	1	5
	No	19	95
Telangiectasia	Yes	1	5
	No	19	95

χ^2: Chai square test.
HS: High significant (P<0.001)
S: Significant (P<0.05)

Table (5): Clinical response among the study group:

Variable		(IL vit. D) (*n*=20)	
		No	**%**
Clinical response:	A0	3	15
	A1	15	75
	A2	2	10
	A3	0	0
	A4	0	0
	A5	0	0

χ^2: Chai square test. **HS:** High significant (P<0.001)

Case Presentation:

Case1: Male (19 years old) with patchy alopecia areata. (A) First visit patch of Alopecia Areata clinical view. (B) Dermoscopic image of First visit with black (red circle) and yellow (yellow circle) dots. (C) After three months clinically. (D) During the most recent visit, the dermoscopic image displayed upright hair growth (green arrow) (mild improvement) (Figure 1).

Case2: Male (33 years old) with patchy alopecia areata. (A) First visit patch of Alopecia Areata clinical view. (B) Black dots in the first visit's dermoscopic image (red circle) and yellow dots (yellow circle) and short broken hair (black arrow). (C) After three months clinically. (D) Dermoscopic image from last visit displaying hair growth in an upright position (green arrow) grey hair (orange arrow). (mild improvement) Figure (2).

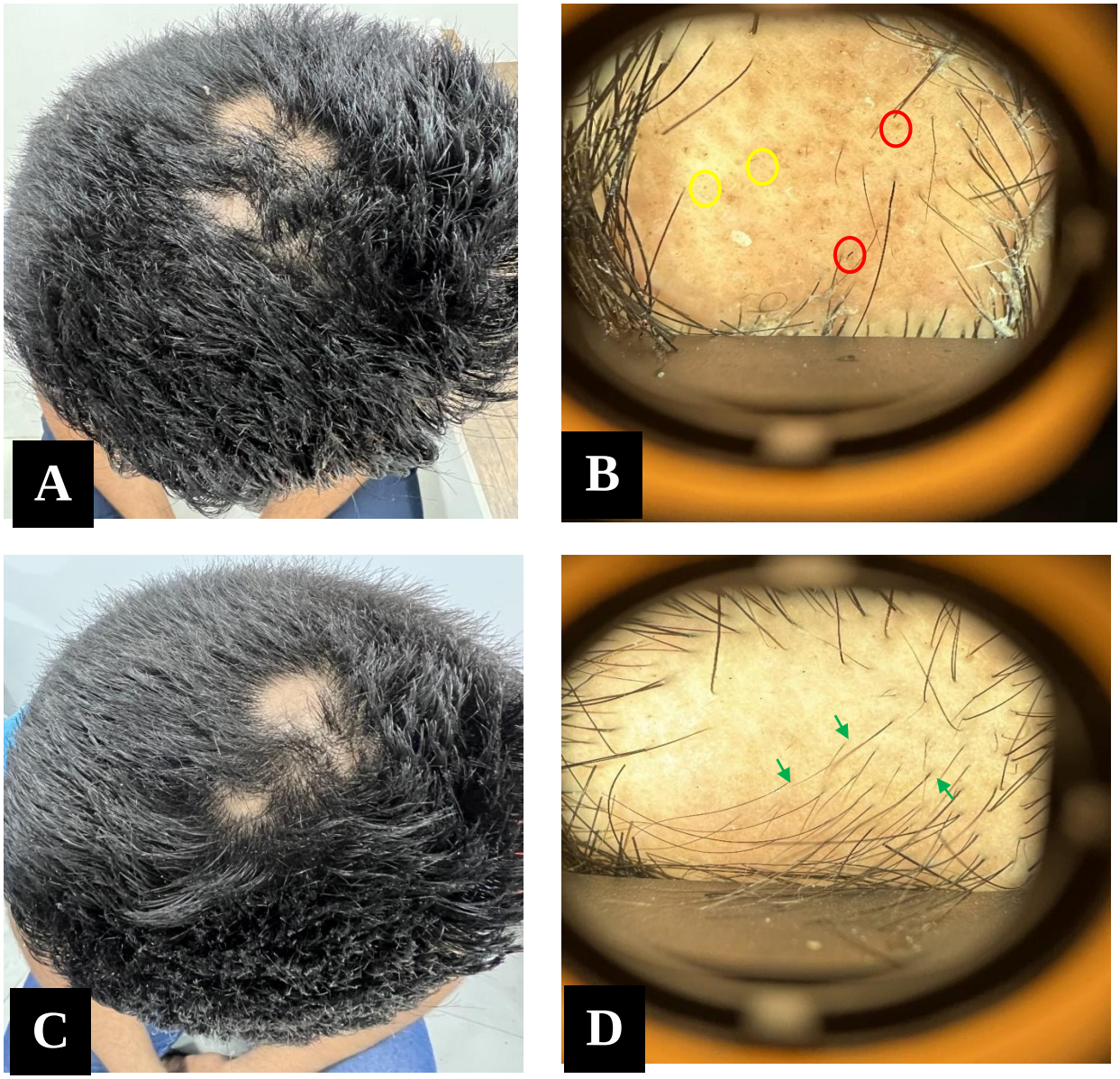

Figure 1: 19 years old male patient treated by intralesional vit D

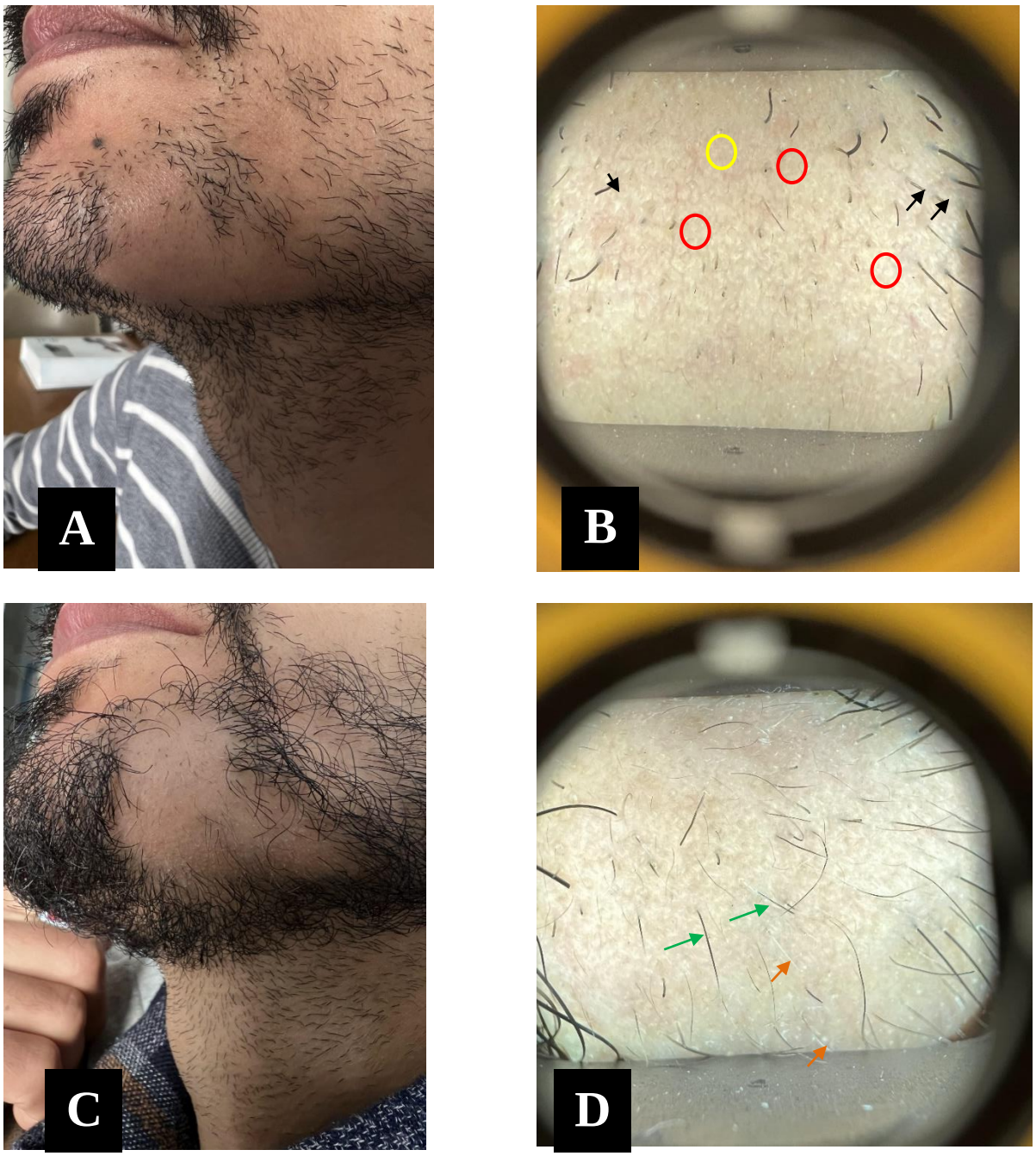

Figure 2: 33 years old male patient treated by intralesional vit D.

DISCUSSION

We conducted a clinical trial study on 20 patients with a mean age of 23.5 (± SD11.4; range7–41) years. At baseline, all patients had mild to moderate AA. The mean disease duration was 12.2(± SD11.39; range 1–32) months. It was discovered that none of the patients had any family history of AA of any kind. 25% of our patients were females and 75% males, no nail abnormalities, and no previous treatment was taken by patients before our study.

This study showed thatthere was no statistical significance change in SALT score among group patients post treatment compared to pretreatment, regarding clinical response there was 10% of cases (2 patients) shows hair regrowth by >25% (A2) and majority of patients 75% (15patients) shows minimal hair regrowth by <25% (A1), 15% of cases (3 patients) shows no improvement at all (A0).

Regarding adverse effects of treatment, there was erythema, itching and pain assessed among studied cases (20%, 15% and 15% respectively). Atrophy and telangiectasia were found among 5% in cases.

Regarding the use of vitamin D3, a few published studies were found that discuss the effectiveness of topical D3 analogues in the management of Alopecia Areata, which raises questions about the efficacy of the use of vitamin D itself as intralesional treatment.

Molinelli et al. [1] in one study, for instance, 35 patients who were Caucasian and had a mean age of 32.3 (± SD 8.1; range 19–56) years were included. All patients had mild to moderate AA (AGS 2-4) at baseline. With a mean of 27.1 (± SD 10.01) years, the range of AA's onset age was 11–53 years. Eight patients (22.9%) had a family history of any type of AA. With a mean of 27.1 (± SD 10.01) years, the range of AA's onset age was 11–53 years. Eight patients (22.9%) had a family history of any type of AA. The topical vitamin D analogue has a lower adverse effect profile and is both safe and efficacious for treating scalp AA. Likewise, patients were monitored for a full year, with the calcipotriol group experiencing a decreased rate of relapse.

Similarly, three patients receiving clobetasol propionate treatment for their AA regions reported experiencing moderate pruritus and telangiectasia. Two patients who used calcipotriol 0.005% ointment on their patches reported slight erythema and itching **[1].**

Our results are supported by **Rashad et al [14]** in terms of clinical response, the groups that received intralesional vitamin D3 and intralesional saline differed statistically significantly ($p < 0.01$). With the intralesional vitamin D3 group exhibiting superior outcomes. This is the first study that discusses treating patchy alopecia areata with intralesional vitamin D3.

None of the subjects in the study experienced severe adverse effects that required them to quit their medication in 66.7% of patients receiving intralesional vitamin D3 group treatment, minimally uncomfortable injections were reported. In 33.3% of individuals receiving intralesional vitamin D3 group treatment, pinpoint bleeding at the injection site was noted. Finally, 4 (13.3%) of the intralesional vitamin D3 group's participants experienced a vasovagal event **[14]**.

CONCLUSIONS

However, according to the small number of patients in this study, more extensive studies are needed to confirm the results.

Intralesional Vitamin D (cholecalciferol) is a mild effective treatment of Alopecia Areata.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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None declared

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