A randomized comparative study between intralesional vitamin D3 and intralesional triamcinolone acetonide in the treatment of alopecia areata

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Background
Alopecia areata (AA) is a common hair loss disorder. Despite the availability of various treatment options, no single agent consistently cures this condition. Vitamin D, with its immunomodulatory effects, emerges as a promising treatment avenue for AA.
Objective
To assess the safety and efficacy of intralesional vitamin D3 compared with intralesional triamcinolone acetonide (TAC) in AA. Also, the treatment response should be analyzed according to serum vitamin D3 levels.
Patients and methods
This randomized controlled trial involved 40 patients aged 12 years and older with patchy active AA involving less than 50% of the scalp. The patients were randomized into two groups: group A received intralesional TAC, and group B received intralesional vitamin D3. Each patient underwent four treatment sessions and two follow-up sessions at monthly intervals. Serum vitamin D3 levels were assessed at the baseline. The regrowth score (RGS) was used to assess clinical improvement.
Results
Both groups showed significant improvement in mean RGS at the 16th and 20th weeks compared with the fourth week ($P<0.001$; for both groups at the 16th and 20th weeks). By the 20th week, the mean RGS reached 3.05 in group A and 2.55 in group B ($P=0.398$). No significant difference was found between good and poor responders regarding vitamin D levels. Trichoscopic signs of activity improved significantly in both groups, and both treatment modalities were safe, with minor side effects.
Conclusion
Intralesional vitamin D is comparable in efficacy and safety to intralesional TAC in patchy AA of the scalp. Also, the response to treatment was insignificantly influenced by the level of serum vitamin D.

Keywords:
alopecia areata, intralesional triamcinolone acetonide, intralesional vitamin D3, trichoscopy

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Introduction

Alopecia areata (AA) is one of the most common hair loss disorders with a wide presentation, ranging from a focal patch to a complete loss of all body hair with systemic comorbidities [1].

Steroids, administered either topically or intralesionally, remain the traditional first-line therapy for AA. Unfortunately, steroids are broad-spectrum immunosuppressants, and many patients fail to achieve complete response or experience relapses shortly after discontinuing treatment. Moreover, steroids are often limited by their side effects, which preclude their prolonged use or application to large areas [2]. Calcipotriol, the topical form of vitamin D3, has garnered attention for treating AA due to its comparable effectiveness to topical steroids with fewer side effects [3]. Additionally, the injectable form of vitamin D3 has shown success in treating various dermatologic conditions, including viral warts [4].

The nonclassical roles of vitamin D involve a complex influence on the immune system [5]. This explains why many autoimmune disorders exhibit low vitamin D levels [6]. Ample evidence shows that serum vitamin D is lower in AA, compared with the general population [7]. Vitamin D has been found to inhibit the activation of the Th1 axis, suppressing the release of key

inflammatory mediators such as INF-γ [8]. Vitamin D also switches off the JAK-STAT pathway, putting an additional layer of block on the downstream signaling of cytokines [9]. Also, vitamin D stabilizes important cells involved in the pathogenesis of AA, particularly cytotoxic $CD8^+$ T cells, Th17, and mast cells [8,10].

In light of the absence of a reliable and effective therapy for AA, it becomes crucial to investigate novel treatment approaches capable of modifying the disease course and preventing recurrent episodes. To the best of our knowledge, this study represents the first comparison between intralesional steroids and intralesional vitamin D in treating active AA.

This study aimed to evaluate the safety and efficacy of intralesional vitamin D3 in the treatment of AA compared with intralesional triamcinolone acetonide (TAC); and to interpret the response to treatment with regard to the level of serum vitamin D3.

Patients and methods

This was an open-label prospective randomized trial that was carried out between December 2022 and November 2023 at the Outpatient Dermatology Clinic. A total of 40 patients with AA were enrolled.

The study protocol was approved by the local ethics committee (IRB NO: 00012098–FWA NO:00018699; Serial Number: 0107377). ClinicalTrials.gov ID NCT04660786. The study was performed in accordance with the principles of the Declaration of Helsinki. Written informed consent for participation in the study was obtained from all patients.

Inclusion criteria: patients with trichoscopically active patchy AA aged more than or equal to 12 years; sex: males and females; site: scalp; active AA by dermoscopy; and patchy AA (involvement <50%). Exclusion criteria: any systemic or skin diseases associated with hair loss; pregnant or lactating women; bleeding or coagulation disorders; immunocompromised patients; known hypersensitivity to vitamin D3; patients who received systemic or topical treatment for AA in the last month; medications that could be related to hair loss (e.g. anticoagulants, retinoids, anticonvulsants, and antidepressants); patients who have taken vitamin D supplements in the last 6 months; patients treated with topical vitamin D analogs; and patients with diseases known to alter vitamin D level as autoimmune diseases, liver, renal diseases or obesity (defined as BMI≥25).

A total sample size of n=40 was calculated using Power Analysis and Sample Size Software (PASS 2020) "NCSS, LLC. Kaysville, Utah, USA, ncss.com/software/pass" taking into consideration an assumed effect size (a minimally clinically important difference) of 20%, 95% level of confidence, compliance ratio (1 : 1), and power of 80% using χ^2 test. The following formula was used:

$$n=N\times[Z^2\times p\times(1\text{-}p)/e^2]/[N\text{–}1+(Z^2\times p\times(1\text{-}p)/e^2].$$

where N=population size, Z=critical value of the normal distribution at the required confidence level, P=sample proportion, e=margin of error.

All of the 40 patients were subjected to full history taking, complete dermatologic examination, and trichoscopic examination (DermLite DL4; 3 Gen, USA; ×10) to assess signs of activity: black dots, broken hairs, exclamation mark hairs, and Pohl-Pinkus constrictions (monilethrix-like hair). A venous blood sample was analyzed for 25-hydroxy vitamin D3 using a commercial enzyme-linked immunosorbent assay. Vitamin D was considered deficient at a level less than 20 ng/ml [11].

Patients were randomized into treatment groups using blocked randomization. This service was used to generate the randomization list, which was printed beforehand. https://www.sealedenvelope.com/simple-randomiser/v1/lists. Block sizes: 2,4,6–List length: 40. Patients were allocated in a 1 : 1 ratio into two groups, 20 patients each:

(1) Group A received intralesional injections of TAC [5 mg/ml; max 20 mg per session (Epirelefan 40 mg/ml; EIPICO, Cairo, Egypt)].
(2) Group B received intralesional injections of vitamin D3 [2.5 mg/ml from an aqueous preparation of cholecalciferol (Devarol 200 000 IU/2 ml; Memphis, Egypt; max 4 ml per session)].

Injections were done using disposable insulin syringes 1 ml U-100 30 G. Injections were done by 0.1 ml/injection every 1 cm. A mixture of 2.5% lidocaine and 2.5% prilocaine was used as a topical anesthetic for 30–60 min under occlusion before every session (Pridocaine, Global Napi Pharmaceuticals, Egypt).

Patients received four treatment sessions and two follow-up sessions at monthly intervals. At the baseline and thereafter, lesions were photographed using a cell phone camera (iPhone 13 pro, Apple, USA) and DermLite DL4.

An independent blinded investigator evaluated the outcome using the five-point scoring system of regrowth score (RGS) [12] (0=regrowth <10%; 1=regrowth 11–25%; 2=regrowth 26–50%; 3=regrowth 51–75%; 4:=regrowth >75%). Patients with an RGS 0–2 were considered poor responders, and patients with an RGS 3–4 were considered good responders.

Statistical analysis

Statistical analysis was conducted using Statistical Package for the Social Sciences (SPSS), version 20 (IBM, Chicago, Illinois, USA). Qualitative variables were described using numbers and percentages. Quantitative variables were described using range (minimum and maximum), mean, SD, median, and interquartile range.

The χ^2 and Fisher exact tests assessed associations between categorical variables, with Fisher used for small samples. The Friedman test, a nonparametric method, detected differences in treatments across multiple attempts, suitable for repeated measures data without normality. Monte Carlo correction adjusted *P* values for multiple comparisons. The Mann–Whitney test compared differences between two independent groups with ordinal or nonnormally distributed continuous data. The Kruskal–Wallis test compared population medians of more than two independent groups, followed by Dunn's multiple comparisons test for specific group differences. The Spearman correlation test measured the association between ranked variables. *P* values less than 0.05 were considered statistically significant.

Results

Demographics and baseline patient characteristics

This study involved 40 patients with a mean age of 26.4 years. Group A and group B (20 patients each) were matched in terms of age, sex, disease duration, lesion size, baseline serum vitamin D3, and family history. There was a statistical difference between the two groups regarding the area affected (P=0.010). The occipital area was the most involved in both groups, followed by the temporal area. The mean level of serum vitamin D in group A was 18.06 ±8.13 and 16.52±5.71 ng/ml in group B. Vitamin D was found deficient in 26/40 (65%) of the total sample, with 12/20 (60%) of group A and 14/20 (70%) of group B showing laboratory signs of vitamin D deficiency with a serum level less than 20 ng/ml (Table 1).

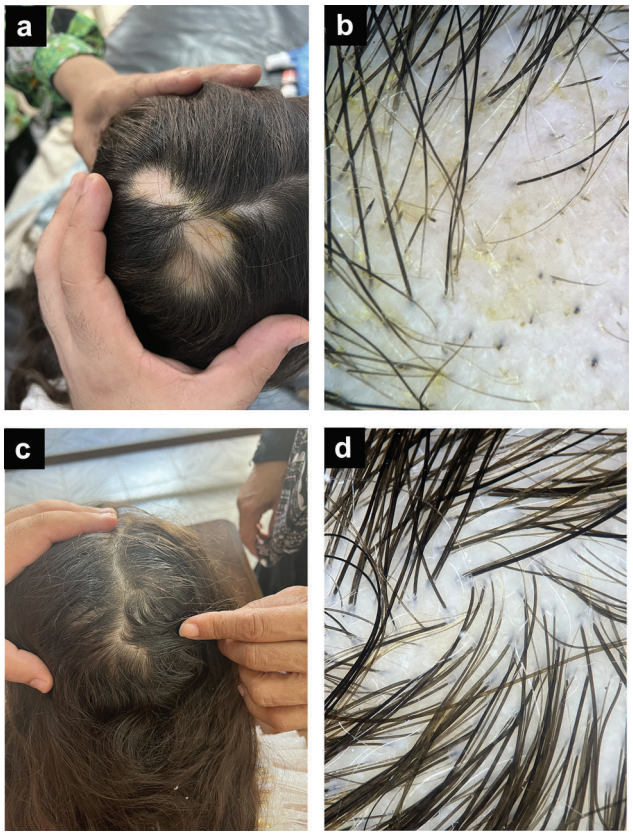
Clinical response and mean regrowth score

There was no statistically significant difference between both groups in terms of the mean RGS across all sessions, although group A had a higher mean than group B. The mean RGS increased steadily in both groups from the baseline to the 20th week, reaching 3.05±1.0 in group A and 2.55±1.47 in group B. Both groups showed a statistically significant improvement in the mean RGS in the 16th and 20th weeks, compared with the 4th week (P<0.001) (Table 2).

Figure 1 shows a good response to intralesional vitamin D3, while Fig. 2 shows a poor response to the same treatment. Figure 3 shows a good response to intralesional TAC, while Fig. 4 shows a patient with a poor response to the same modality.

No statistically significant association was observed between the clinical response and patient age, sex, serum vitamin D, lesion size, disease duration, or family history in both groups. However, in both

Figure 1



Patient with parietal AA with a good response to intralesional vitamin D. (a) Baseline. (b) Baseline trichoscopy (×10): black dots, broken hairs, and exclamation mark hairs. (c) Week 20 regrowth score 4. (d) Week 20 trichoscopy: normal terminal hair regrowth. AA, alopecia areata.

Table 1 Demographics and baseline patient characteristics of both groups

	Total (*N*=40) [*n* (%)]	Group A (*N*=20) [*n* (%)]	Group B (*N*=20) [*n* (%)]	Test of significance	*P*
Sex					
Male	29 (72.5)	14 (70.0)	15 (75.0)	χ^2=0.125	0.723
Female	11 (27.5)	6 (30.0)	5 (25.0)		
Age (years)					
Range	12.0–64.0	12.0–44.0	12.0–64.0	*U*=190.50	0.799
Mean±SD	26.425±12.01	26.28±10.55	26.68±13.47		
Duration (months)					
Range	0.5–48	1.50–48.0	0.50–24.0	*U*=146.50	0.149
Mean±SD	7.725±9.89	9.98±12.44	5.48±5.94		
Site					
Frontal	7 (17.5)	0	7 (35.0)	χ^2=10.507*	^{MC}P=0.010*
Parietal	5 (12.5)	4 (20.0)	1 (5.0)		
Temporal	10 (25)	7 (35.0)	3 (15.0)		
Occipital	18 (45)	9 (45.0)	9 (45.0)		
Size (cm^2)					
Range	1.17–110	1.76–110.0	1.17–74.0	*U*=142.50	0.121
Mean±SD	25.629±27.84	34.36±33.28	16.90±17.98		
Vitamin D3 (ng/ml)					
Range	7.50–39.74	7.50–39.74	7.50–26.60	*U*=184.0	0.678
Mean±SD	17.29±6.98	18.06±8.13	16.52±5.71		
Patients <20 ng/ml	26 (65.0)	12 (60)	14 (70)	χ^2=0.440	0.507
Patients ≥20 ng/ml	14 (35)	8 (40)	6 (30)		
Family history of alopecia areata					
Negative	32 (80)	15 (75.0)	17 (85.0)	χ^2=0.625	^{FE}P=0.695
Positive	8 (20)	5 (25.0)	3 (15.0)		

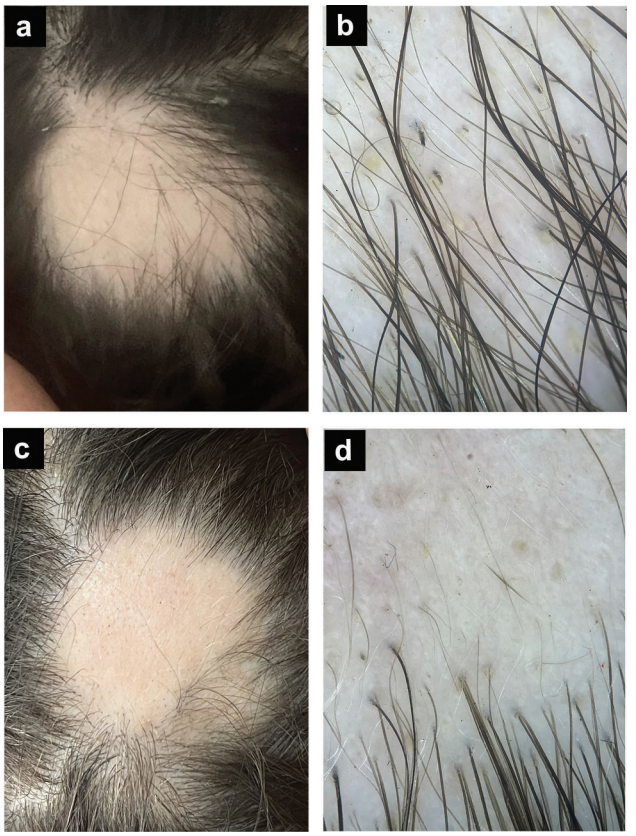
FE, Fisher exact; MC, Monte Carlo; *U*, Mann–Whitney test; χ^2, χ^2 test. Group A: patients receive an intralesional injection of triamcinolone acetonide (5 mg/ml). Group B: patients receive an intralesional injection of vitamin D3 (2.5 mg/ml). *P*: *P* value for comparing between the two studied groups. **P* value less than 0.05 is considered statistically significant.

Table 2 Comparison between both groups according to regrowth score

Weeks	Group A (*N*=20)		Group B (*N*=20)		Test of significance	*P*
4						
Range	0.0–2.0		0.0–1.0			
Median	0.50		0.0		*U*=172.00	0.461
Mean	0.60±0.68		0.40±0.50			
8						
Range	0.0–3.0		0.0–3.0			
Median	1.0		1.0		*U*=158.00	0.265
Mean	1.40±1.05		1.00±1.03			
12						
Range	0.0–4.0		0.0–4.0			
Median	2.0		1.0		*U*=149.50	0.174
Mean	2.05±1.05		1.50±1.32			
16						
Range	1.0–4.0		0.0–4.0		*U*=152.50	0.201
Median	3.0		2.0			
Mean	2.85±0.99		2.20±1.54			
20						
Range	1.0–4.0		0.0–4.0		*U*=168.00	0.398
Median	3.0		3.0			
Mean	3.05±1.00		2.55±1.47			
P_0 (4–16)	Fr=71.285*	<0.001*	Fr=62.118*	<0.001*		
P_1 (4–20)		<0.001*		<0.001*		

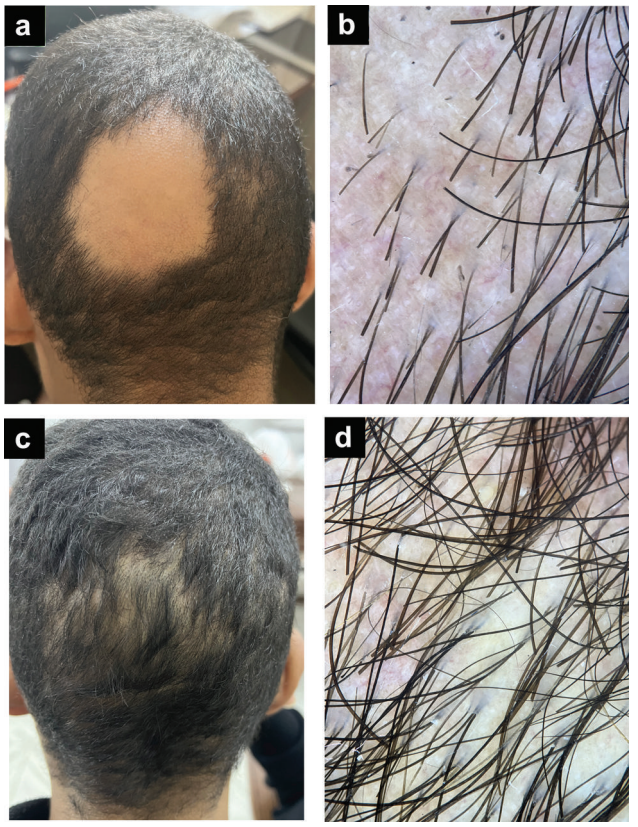
U, Mann–Whitney test. Fr, Friedman test, significance between periods was done using post-hoc test (Dunn's). Group A: patients receive an intralesional injection of triamcinolone acetonide (5 mg/ml). Group B: patients receive an intralesional injection of vitamin D3 (2.5 mg/ml). *P*: *P* value for comparing between the studied sessions. P_0: *P* value for comparing between week 4 and week 16. P_1: *P* value for comparing between week 4 and week 20. **P* value less than 0.05 is considered statistically significant.

Figure 2



Patient with occipital AA with a poor response to intralesional vitamin D. (a) Baseline. (b) Baseline trichoscopy (×10): black dots and broken hairs. (c) Week 20 regrowth score 0. (d) Week 20 trichoscopy: disappearance of broken hairs and few black dots. AA, alopecia areata.

Figure 3



Patient with occipital AA with a good response to intralesional triamcinolone acetonide. (a) Baseline. (b) Baseline trichoscopy (×10): black dots, broken hairs, and exclamation mark hairs. (c) Week 20 regrowth score 4. (d) Week 20 trichoscopy: no signs of activity with improved hair density. AA, alopecia areata.

groups, the larger the lesion, the less likely the response to treatment. Regarding the impact of lesion site, in group A, no statistically significant relation was found between treatment response and different lesion sites. In group B, on the other hand, frontal and temporal lesions were associated with a statistically significant better treatment response (RGS mean of 2.86±1.21 and 3.33±1.15, respectively), while occipital lesions responded poorly (mean RGS 1.11±1.27) (P=0.019) (Tables 3 and 4).

Good and poor responders in the 16th week were analyzed according to the level of their serum vitamin D level. There was no significant difference between good and poor responders in relation to baseline serum vitamin D levels. In group A, 6/8 (75%) with normal serum vitamin D3 were good responders, while 7/12 (58.33%) with vitamin D deficiency achieved the same response. This means that patients with normal vitamin D are insignificantly more likely to show a good response to intralesional steroids (odds ratio=2.143, 95% confidence interval=0.299–15.355). In group B, 7/14 (50%) of patients with vitamin D deficiency were good responders, while 1/6 (16.66%) of patients with normal serum vitamin D achieved the same response. This means that patients with vitamin D deficiency are insignificantly more likely to show a good response to intralesional vitamin D (odds ratio=5, 95% confidence interval=0.459–54.513) (Table 5).

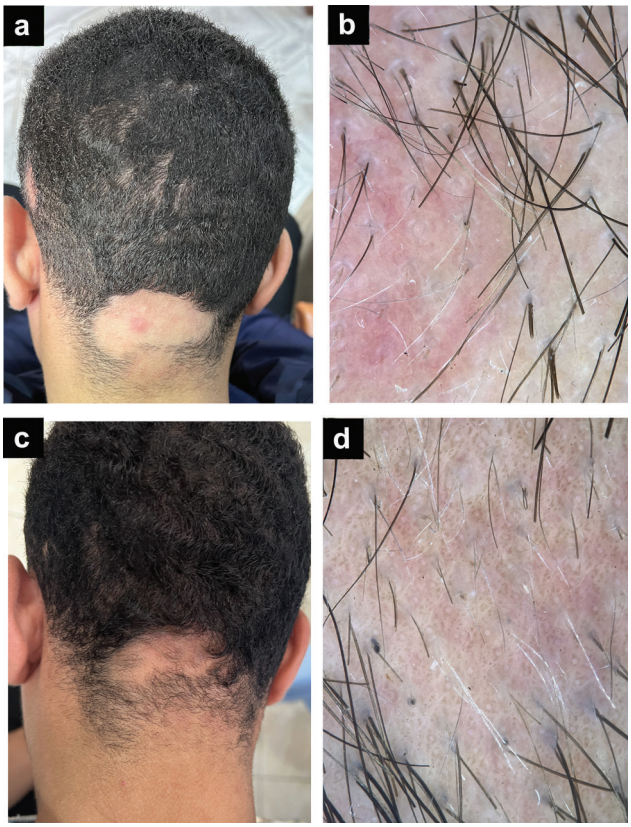
Trichoscopic response to treatment

Trichoscopic signs of disease activity improved from the baseline to the 20th week. Black dots were present in all patients in both groups, broken hairs in 85% of each group, while the least commonly observed exclamation marks were in almost half of the patients. Of note, the onset of trichoscopic improvement in these three signs was earlier in group A than in group B (Table 6).

Safety profile

Burning pain during the injection was reported by 18/20 (90%) of patients in group A, compared with 2/20 (10%) in group B. This difference was statistically significant (P<0.001). An itchy sensation in the

Figure 4



Patient with occipital AA with a poor response to intralesional triamcinolone acetonide. (a) Baseline. (b) Baseline trichoscopy (×10): broken hairs. (c) Week 20 with regrowth score 2. (d) Week 20 trichoscopy: black dots and broken hairs. AA, alopecia areata.

injection site was reported by 2/20 (10%) of patients in group A, compared with 8/20 (40%) of patients in group B, which again was statistically significant (P=0.028). A tender swelling in the injection site was reported by 2/20 (10%) of patients in group A, compared with 13/20 (65%) in group B. This difference reached statistical significance (P<0.001).

Discussion

The role of vitamin D in AA is receiving growing attention since the discovery of the role of VDR in follicle cycling and the successful treatment of many AA patients with the topical vitamin D analog (calcipotriol) and oral vitamin D [13]. Furthermore, more light has been shed on the noncalcemic roles of vitamin D in the body, especially its function as an immunomodulator [14]. To the best of our knowledge, this is a novel study that compared the efficacy of intralesional steroids to intralesional vitamin D in the treatment of active AA.

Interestingly, 65% of patients fulfilled the laboratory criteria of vitamin D deficiency, 60% in group A and 70% in group B. Vitamin D deficiency is defined as a level less than 20 ng/ml, according to the US Endocrine Society [11]. This finding is consistent with a review article by Lin published in 2019 that suggests an association between AA and low serum vitamin D [9]. More specifically, El-Mongy *et al.* [15] confirmed this observation in Egyptian patients, citing higher prevalence of vitamin D deficiency in female patients with AA, compared with male patients. VDRs are expressed by multiple immunocytes, including different T cell subtypes, B cells, and macrophages, which play a crucial role in autoimmune disorders like AA [16].

Table 3 Relationship between regrowth score in week 16 and baseline patient characteristics in each group

	Group A (N=20)		Group B (N=20)	
	N	Regrowth score (mean±SD)	N	Regrowth score (mean±SD)
Sex				
Male	14	2.93±1.07	15	2.40±1.55
Female	6	2.67±0.82	5	1.60±1.52
U (P)		U=33.50 (P=0.494)		U=26.50 (P=0.349)
Site				
Frontal	0	–	7	2.86±1.21
Parietal	4	3.0±0.82	1	4.0†
Temporal	7	2.57±0.98	3	3.33±1.15
Occipital	9	3.00±1.12	9	1.11±1.27
H (P)		H=0.919 (P=0.632)		H=7.935* (P=0.019*)
Family history of alopecia areata				
Negative	15	2.73±1.03	17	2.0±1.54
Positive	5	3.20±0.84	3	3.33±1.15
U (P)		U=28.00 (P=0.445)		U=12.50 (P=0.179)

U, Mann–Whitney test. H, H for Kruskal–Wallis test, pairwise comparison between each two groups was done using post-hoc test (Dunn's for multiple comparisons test). Group A: Patients receive an intralesional injection of triamcinolone acetonide (5 mg/ml). Group B: Patients receive an intralesional injection of vitamin D3 (2.5 mg/ml). P: P value for relation between clinical regrowth score in session 6 with sex and site.
†Excluded from the comparison due to a small number of cases (N=1). *Statistically significant at P value less than or equal to 0.05.

Table 4 Correlation between regrowth score in week 16 and baseline patient characteristics in each group

	Group A (*N*=20)		Group B (*N*=20)	
Parameters	r_s	*P*	r_s	*P*
Age (years)	0.198	0.403	–0.390	0.089
Duration (months)	–0.049	0.836	0.092	0.699
Vitamin D3 (ng/ml)	0.098	0.680	–0.080	0.737
Size (cm^2)	–0.174	0.464	–0.285	0.223

*r*s, Spearman coefficient. Group A: patients receive an intralesional injection of triamcinolone acetonide (5 mg/ml). Group B: patients receive an intralesional injection of vitamin D3 (2.5 mg/ml).

The two groups showed a comparable mean RGS increase throughout all sessions, with an insignificantly higher RGS in group A. Group B had a delayed onset of improvement and insignificantly continued improvement during the follow-up sessions. This suggests that vitamin D has a delayed and sustained response owing to its fat-solubility nature, which lets the tissues store it and slowly release it for longer periods [17].

In the 16th week, the mean RGS for group A was 2.85 ±0.99. Similarly, Ganjoo and Thappa evaluated the efficacy of intralesional injections of TAC (5 mg/ml) on 60 patients with patchy AA. By the 16th week, their mean RGS was 3.59±0.69. Their better results could be attributed to recruiting a higher number of patients (60 patients). They stated that those who did not reach RGS 4 could have had low levels of thioredoxin

Table 5 Association between serum vitamin D level and the type of response at week 16

	Poor responders (regrowth score 0–2) [*n* (%)]	Good responders (regrowth score 3–4) [*n* (%)]	*P*	OR (LL–UL 95% CI)
Group A (*N*=20)				
Vitamin D3 (ng/ml)				
<20	5 (41.67)	7 (58.33)	0.448	0.467 (0.065–3.344)
≥20	2 (25)	6 (75)		2.143 (0.299–15.355)
Group B (*N*=20)				
Vitamin D3 (ng/ml)				
<20	7 (50)	7 (50)	0.187	5.000 (0.459–54.513)
≥20	5 (83.33)	1 (16.66)		0.200 (0.018–2.181)

CI, confidence interval; LL, lower limit; OR, odd's ratio; UL, upper limit. Group A: patients receive an intralesional injection of triamcinolone acetonide (5 mg/ml). Group B: patients receive an intralesional injection of vitamin D3 (2.5 mg/ml).

Table 6 Comparison between the two studied groups according to black dots, broken hair, and exclamation marks

	Total (*N*=40) [*n* (%)]	Group A (*N*=20) [*n* (%)]	Group B (*N*=20) [*n* (%)]	χ^2	*P*
Black dots					
Week 0	40 (100.0)	20 (100.0)	20 (100.0)	–	–
Week 4	38 (95.0	18 (90.0)	20 (100.0)	2.105	FE*P*=0.487
Week 8	28 (70.0)	14 (70.0)	14 (70.0)	0.000	1.000
Week 12	21 (52.5)	10 (50.0)	11 (55.0)	0.100	0.752
Week 16	14 (35.0)	8 (40.0)	6 (30.0)	0.440	0.507
Week 20	12 (30.0)	6 (30.0)	6 (30.0)	0.000	1.000
Broken hair					
Week 0	34 (85.0)	17 (85.0)	17 (85.0)	0.000	FE*P*=1.000
Week 4	32 (80.0)	15 (75.0)	17 (85.0)	0.625	FE*P*=0.695
Week 8	29 (72.5)	14 (70.0)	15 (75.0)	0.125	0.723
Week 12	23 (57.5)	12 (60.0)	11 (55.0)	0.102	0.749
Week 16	17 (42.5)	9 (45.0)	8 (40.0)	0.102	0.749
Week 20	14 (35.0)	7 (35.0)	7 (35.0)	0.000	1.000
Exclamation marks					
Week 0	21 (52.5)	10 (50.0)	11 (55.0)	0.100	0.752
Week 4	20 (50.0)	9 (45.0)	11 (55.0)	0.400	0.527
Week 8	14 (35.0)	5 (25.0)	9 (45.0)	1.758	0.185
Week 12	8 (20.0)	3 (15.0)	5 (25.0)	0.625	FE*P*=0.695
Week 16	6 (15.0)	4 (20.0)	2 (10.0)	0.784	FE*P*=0.661
Week 20	6 (15.0)	4 (20.0)	2 (10.0)	0.784	FE*P*=0.661

χ^2, χ^2 test; FE, Fisher exact. Group A: patients receive an intralesional injection of triamcinolone acetonide (5 mg/ml). Group B: patients receive an intralesional injection of vitamin D3 (2.5 mg/ml). *P*: *P* value for comparing between the two studied groups.

reductase, the enzyme that mediates steroid response in the outer root sheath [12].

Group B also responded favorably. One month after the third session (the 12th week), the mean RGS for group B was 1.50±1.32. Likewise, Rashad and colleagues evaluated the efficacy of intralesional vitamin D3 and found that after the third session, the mean RGS for the vitamin D group was 3±1.31. In their study, they recruited a higher number (30 patients) but treated them for three sessions only, with further 3 months as a follow-up to assess long-term benefits and detect relapses [18].

The intriguing question arises: does vitamin D require a longer duration to sustain a more robust response that could potentially surpass group A if patients were followed up for an extended period? Interestingly, Molinelli and colleagues reported that calcipotriol is insignificantly more effective than clobetasol in treating AA, with a faster response. In their study, RGS 4 was observed in 68.77% of the calcipotriol group compared with 62.86% in the clobetasol group after 24 weeks [3]. The faster response in their study may be attributed to the fact that calcipotriol is a synthetic analog of the active form of vitamin D3, necessitating no additional activation in vivo [19]. In contrast, cholecalciferol, in its injectable form, remains inactive and relies on subsequent activation by skin hydroxylases. These enzymatic activities can be influenced by various factors, including ultraviolet radiation [20].

Another important factor is the level of serum vitamin D, which has been proposed to affect AA [9]. In the present work, there was no significant difference between good and poor responders regarding vitamin D levels. In group A, patients with normal vitamin D had 2.13 times the odds of having a good response compared with patients with low vitamin D. On the other hand, in group B, patients with low vitamin D had five times the odds of having a good response compared with patients with normal vitamin D. Many studies reached a similar conclusion that patients with low serum vitamin D would have higher benefit from calcipotriol than patients with normal vitamin D [21,22].

To determine which patients would benefit from steroid monotherapy, vitamin D monotherapy, or a combination of both, a randomized controlled trial is needed that assigns patients to different treatment groups based on their vitamin D levels and compares their responses over time. Abdel Fattah and Darwish pointed out that a complete cure of AA in patients treated with phototherapy and who are deficient in vitamin D may be possible after replenishing their vitamin D stores. According to their observations, phototherapy led to increased serum levels of vitamin D through activation of 1α-hydroxylase. Notably, injectable vitamin D remains inactive and requires further activation in the skin to exert its immunologic functions [23]. This raises an important question: could nonresponders to vitamin D supplementation benefit from auxiliary phototherapy sessions to facilitate the conversion of vitamin D into its active state?

Trichoscopic findings that correlate positively with AA activity are broken hairs, black dots, and exclamation mark hairs [24]. Group A and group B were comparable regarding baseline trichoscopic signs of activity. Black dots were present in all patients in both groups, broken hairs in 85% of each group, while the least commonly observed exclamation marks were in almost half of the patients.

The most encountered immediate adverse effect was an intense burning during injection, despite premedication with a topical anesthetic. This pain occurred in 90% of group A and 10% of group B. Similar complaints were documented by Metwally *et al.* [25], who reported that 66% of their patients in the steroid group experienced burning pain lasting only a few minutes.

In group A, no patient presented with trichoscopic signs of skin atrophy or telangiectasia. In contrast, skin atrophy was observed by Ganjoo and Thappa [12] in 18.50% of patches in the 12th week despite using a concentration of 5 mg/ml and a maximum of 3 ml.

As for group B, a substantial proportion (65%) of patients complained of a tender swelling at the site of injection that lasted for 2–10 days. Another complaint was an itchy sensation that was relieved by an antihistamine tablet for 1 or 2 days (40% of patients). This was also reported in patients with warts treated with intralesional vitamin D. This could be explained by the fact that vitamin D is an oily substance that causes an inflammatory reaction with resultant edema and pruritus [26]. Rashad *et al.* [18] reported that 13.3% of patients had a vasovagal attack only in the vitamin D group, which was not reported in the present study. In general, all of these side effects were self-limited, and no patient dropped because of intolerability.

This study showcased the efficacy and safety of intralesional vitamin D in treating AA, compared with steroids. This finding could be significant for patients and clinicians seeking alternative therapies. Also, future studies should group patients according to their serum vitamin D level to see which patients would benefit better from steroid monotherapy, vitamin D monotherapy, and a combination of both. Also, future studies can compare the convenient topical calcipotriol to the cumbersome intralesional vitamin D. Furthermore, nonresponders to vitamin D might undergo phototherapy sessions to decide if there is an impaired enzymatic activation of vitamin D that benefits from aided ultraviolet catalysis.

Limitations

This study has some potential limitations that should be considered. One limitation is its relatively short duration. It is important to note that AA is a chronic disorder characterized by periods of remission and relapse. Given this context, the study's duration may not fully capture the long-term effects of the treatment modalities being investigated. Another consideration is the lack of patient subgrouping based on serum vitamin D3 levels. By categorizing patients according to their vitamin D3 levels, researchers could have obtained more robust and statistically meaningful insights from the results. Finally, the study did not conduct monthly monitoring of serum vitamin D3 and calcium levels. This monitoring is crucial to establish the biochemical safety profile of intralesional vitamin D3 injections.

Conclusion

Compared with intralesional steroids, intralesional vitamin D3 holds promise as a safe and effective agent in treating patchy active AA. No statistically significant association was found between the type of response and the level of serum vitamin D.

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Conflicts of interest

There are no conflicts of interest.

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