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Intralesional Methotrexate versus Triamcinolone Acetonide for Localized Alopecia Areata (AA) Treatment

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ABSTRACT

Background: Alopecia areata (AA) is a common, immune-mediated cause of non-cicatricial hair loss with unpredictable course and limited durable treatment options. Intralesional triamcinolone acetonide (TrA) remains the standard therapy for localized disease, while methotrexate (MTX) has emerged as a potential alternative due to its immunomodulatory effects. **Objective:** To compare the efficacy and safety of intralesional MTX versus TrA in the treatment of localized AA in adults.

Patients and Methods: In this randomized phase II clinical trial, 50 adults (>18 years) with patchy AA involving <50% of the scalp were equally allocated to intralesional MTX (25 mg/mL; 0.1–0.2 mL/session) or TrA (10 mg/mL; ≤2 mL/session) every 3 weeks for up to four sessions. Severity of Alopecia Tool (SALT) scores, patient satisfaction, and adverse events were assessed at baseline, 3 months, and 6 months. **Results:** Baseline characteristics were comparable between groups. Mean SALT scores improved significantly in both MTX (2.72 ± 1.49 to 0.48 ± 1.42) and TrA (2.88 ± 1.45 to 0.60 ± 1.41) groups by 6 months (both $p < 0.001$), with no significant intergroup difference ($p = 0.389$). High satisfaction was reported in 64.0% (MTX) and 52.0% (TrA) patients. Adverse events differed: hyperpigmentation occurred in 32.0% of MTX patients, while hypopigmentation and atrophy occurred only in the TrA group (8.0% each) ($p = 0.018$). The mean number of sessions was similar (MTX: 3.60; TrA: 3.68).

Conclusions: Intralesional MTX and TrA offer comparable efficacy in localized AA, but their distinct safety profiles—hyperpigmentation with MTX and atrophy with TrA—should guide individualized treatment selection.

Keywords: Alopecia areata, intralesional methotrexate, triamcinolone acetonide, SALT score, hair regrowth.

INTRODUCTION

Alopecia areata (AA) is a prevalent autoimmune disorder characterized by non-scarring hair loss that can manifest as discrete patches, confluent areas, or diffuse thinning. Although any hair-bearing region may be affected, the scalp is most frequently involved. Recurrent or extensive disease can significantly impair patients' quality of life, contributing to psychological distress, altered self-image, and social withdrawal [1]. The pathogenesis is multifactorial, with autoimmune and genetic predispositions playing central roles in the inflammatory targeting of hair follicles [2].

A broad spectrum of therapeutic approaches has been explored for AA, including topical, intralesional, and systemic corticosteroids; photochemotherapy; topical immunomodulators such as diphenylcyclopropenone; and adjunctive agents like anthralin or minoxidil. Despite these options, AA remains therapeutically challenging, with fewer than one in five patients achieving sustained, complete regrowth [3].

For adults with localized disease affecting less than half of the scalp, intralesional corticosteroids remain the first-line intervention, followed by topical corticosteroids, minoxidil, and anthralin [4].

Methotrexate (MTX), a folate antagonist with antiproliferative, anti-inflammatory, and immunomodulatory properties, received U.S. FDA approval in 1971. Beyond its oncologic indications—including keratoacanthoma, cutaneous squamous cell carcinoma, and certain lymphomas—MTX is also employed in inflammatory dermatoses such as nail and plaque psoriasis, pyoderma gangrenosum, and cutaneous Crohn's disease [5]. Both systemic and intralesional MTX have shown encouraging results in AA, with several studies supporting its role as an effective and well-tolerated alternative to intralesional triamcinolone for localized forms of the condition [4].

This study aimed to compare the efficacy and safety of intralesional MTX with intralesional triamcinolone acetonide (TrA) in the management of localized AA in adults.

PATIENTS AND METHODS

Study Design and Setting

This randomized phase II clinical trial was carried out in 50 adult patients with patchy AA at the Dermatology, Venereology, and Andrology Department, Faculty of Medicine, Ain Shams University Hospitals, during the period from October 2024 to March 2025.

Participants

Eligible participants were adults over 18 years of age, of either sex, presenting with patchy AA of the scalp affecting less than 50% of the scalp surface area, and who had not received any AA-specific treatment in the preceding three months.

Exclusion Criteria

Patients were excluded if they were younger than 18 years, pregnant or breastfeeding, had chronic hepatic or hematologic disease, were immunocompromised, or had extensive AA (alopecia

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totalis, alopecia universalis, or scalp involvement >50%). Additional exclusion criteria included recent disease onset (<3 months) or receipt of any AA treatment within the last three months.

Randomization and Group Allocation

Participants were randomly assigned in equal numbers to receive either intralesional TrA or intralesional MTX. All underwent comprehensive history-taking and full general and dermatological examination to document lesion site, size, and number.

Intervention Protocols

Methotrexate group: MTX (25 mg/mL) was injected intradermally at 1 cm intervals under aseptic conditions every three weeks. Each injection site received 0.02 mL, with a maximum total dose per session of 0.1–0.2 mL (2.5–5 mg), using a 30-gauge, 0.5-inch needle attached to an insulin syringe.

Triamcinolone group: Commercial TrA (Kenacort® 40 mg/mL) was diluted to 10 mg/mL and injected intradermally at 1 cm intervals. Each site received 0.05–0.1 mL, with a maximum of 2 mL (20 mg) per session, using the same needle and syringe specifications [Melo DF, Dutra TBS, 2018].

Assessment methods:

Treatment sessions were administered at three-week intervals, with a maximum of four sessions per patient. Evaluations were performed at baseline and at the three-month endpoint.

Evaluation Procedures

Baseline assessment included both clinical and photographic documentation of alopecic patches using a high-resolution digital camera high-resolution digital camera" unless the specific brand and model are critical to the methodology. Follow-up evaluations at three months employed the same methods to ensure consistency. The principal investigator met regularly with co-investigators to review collected data, monitor treatment outcomes, and record any adverse events. Any serious adverse events were reported promptly to the Research Ethics Committee for further review.

Severity Scoring

Disease severity was quantified using the Severity of Alopecia Tool (SALT) score, which measures the percentage of scalp hair loss on a scale from 0 to 100. A score of 0 indicates complete hair retention, whereas 100 represents total scalp hair loss. Scores ≥50 are generally considered indicative of severe disease.

Sample Size

Sample size was determined using the PASS statistical software, with power set at 80% and an alpha error of 5%. Based on prior data [6], an expected effect size of 0.8 was assumed for differences in mean hair regrowth rate between groups. Allowing for a 5% dropout rate, a total of 50 patients (25 per group) was calculated as the minimum required sample size.

Ethical considerations

The protocol was reviewed and approved by the Research Ethics Committee, Faculty of Medicine, Ain Shams University. Written informed consent was obtained from all participants prior to enrolment. The consent process included a clear explanation of the study objectives, procedures, and potential risks, along with explicit permission for anonymized data to be used in publications. Participant confidentiality and privacy were maintained in full accordance with the ethical principles outlined in the Declaration of Helsinki.

Statistical analysis

Data analysis was performed using SPSS version 25 (IBM Corp., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. The Shapiro–Wilk test assessed normality of distribution. For normally distributed variables, comparisons between groups were made using the student's t-test; for non-normally distributed variables, the Mann–Whitney U test was applied. Within-group changes over time for non-parametric data were analyzed using the Wilcoxon signed-rank test. Associations between categorical variables were evaluated using the Chi-square test. A two-tailed p-value <0.05 was considered statistically significant.

RESULTS

There were no statistically significant differences between the MTX and TrA groups in terms of age (P = 0.785) or gender distribution (P = 0.762), **Table 1.**

Table 1: Demographic and Baseline Characteristics of Study Participants

Parameter	Category	MTX (n=25)	TrA (n=25)	Test Results
Age (years)	Mean ± SD	35.32 ± 9.78	36.04 ± 8.75	t: 0.274, p=0.785
	Median (Range)	34.00 (21.00-50.00)	37.00 (20.00-50.00)	
Gender	Female	18 (72.0%)	16 (64.0%)	X^2: 0.092, p=0.762
	Male	7 (28.0%)	9 (36.0%)	

MTX: Methotrexate, TrA: Triamcinolone Acetonide, n: number, SD: Standard Deviation, X^2: Chi-square, t: Student t test.

All patients in both groups presented with acute onset of AA (P = 1.000). The course of disease did not differ significantly between groups, although stationary disease was more frequent in the MTX group and progressive disease more frequent in the TrA group (P = 0.053), **Table 2.**

Table 2: Medical history in study groups.

Parameter	Category	MTX (n=25)	TrA (n=25)	Test Results
Onset	Acute	25 (100.0%)	25 (100.0%)	X^2: 0.000, p=1.000
Course	Stationary	22 (88.0%)	15 (60.0%)	X^2: 3.742, p=0.053
	Progressive	3 (12.0%)	10 (40.0%)	

MTX: Methotrexate, TrA: Triamcinolone Acetonide, n: number, X^2: Chi-square.

No statistically significant differences were detected between groups regarding patch size (P = 0.122), pattern (P = 1.000), nail changes (P = 1.000), or duration of illness (P = 0.263), **Table 3.**

Table 3: Clinical presentation in study groups.

Parameter	Category	MTX (n=25)	TrA (n=25)	Test Results
Size of Patch (cm)	<3 cm	1 (4.0%)	6 (24.0%)	X^2: 4.212, p=0.122
	3 cm	11 (44.0%)	8 (32.0%)	
	>3 cm	13 (52.0%)	11 (44.0%)	
Pattern	Patchy	25 (100.0%)	25 (100.0%)	X^2: 0.000, p=1.000
Nail Changes	Negative	25 (100.0%)	25 (100.0%)	X^2: 0.000, p=1.000
Duration of illness (Months)	Mean ± SD	5.04 ± 1.10	4.64 ± 1.38	t: 1.133, p=0.263
	Median (Range)	5.00 (3.00-7.00)	5.00 (3.00-8.00)	

MTX: Methotrexate, TrA: Triamcinolone Acetonide, cm: centimeters, n: number, SD: Standard Deviation, X^2: Chi-square, t: Student t test.

Baseline SALT scores (P = 0.368), SALT scores after 3 months (P = 0.352), and SALT scores after 6 months (P = 0.389) did not differ significantly between the two groups. However, within-group analysis demonstrated a highly significant reduction in SALT scores from baseline to follow-up in both the MTX and TrA groups (P < 0.001 for each). **Table 4**

Table 4: SALT scores in study groups.

Parameter	Category	MTX (n=25)	TrA (n=25)	Test Results
SALT before	Mean ± SD	2.72 ± 1.49	2.88 ± 1.45	Z: 0.815, p=0.368
	Median (Range)	2.00 (2.00-9.00)	3.00 (2.00-9.00)	
SALT after 3 months	Mean ± SD	2.08 ± 1.41	2.32 ± 1.65	Z: 0.893, p=0.352
	Median (Range)	2.00 (1.00-8.00)	2.00 (0.00-8.00)	
SALT after 6 months	Mean ± SD	0.48 ± 1.42	0.60 ± 1.41	Z: 0.699, p=0.389
	Median (Range)	0.00 (0.00-7.00)	0.00 (0.00-7.00)	
Same group comparison		<0.001*	<0.001*	

SALT: Severity of Alopecia Tool, MTX: Methotrexate, TrA: Triamcinolone Acetonide, n: number, SD: Standard Deviation, Z: Mann-Whitney Test, *: significant p-vlaue.

Side effects showed a statistically significant difference between the two groups (P = 0.018), with hyperpigmentation occurring exclusively in the MTX group (32.0%), and hypopigmentation and atrophy observed only in the TrA group (8.0% each). Patient satisfaction (P = 0.493) and the number of treatment sessions required (P = 0.568) were not significantly different between groups, **Table 5.**

Table 5: Outcome in study groups.

Parameter	Category	MTX (n=25)	TrA (n=25)	Test Results
Patient Satisfaction	High	16 (64.0%)	13 (52.0%)	X^2: 2.401, p=0.493
	Moderate	6 (24.0%)	5 (20.0%)	
	Mild	2 (8.0%)	3 (12.0%)	
	No	1 (4.0%)	4 (16.0%)	
Number of Sessions	Mean ± SD	3.60 ± 0.50	3.68 ± 0.48	Z: 0.485, p=0.568
	Median (Range)	4.00 (3.00-4.00)	4.00 (3.00-4.00)	
Side Effects	No	15 (60.0%)	20 (80.0%)	X^2: 13.714, p=0.018*
	Hyperpigmentation	8 (32.0%)	0 (0.0%)	
	Erythema	1 (4.0%)	1 (4.0%)	
	Erosions	1 (4.0%)	0 (0.0%)	
	Hypopigmentation	0 (0.0%)	2 (8.0%)	
	Atrophy	0 (0.0%)	2 (8.0%)	

MTX: Methotrexate, TrA: Triamcinolone Acetonide, n: number, SD: Standard Deviation, X^2: Chi-square, Z: Mann-Whitney Test, *: significant P-value.

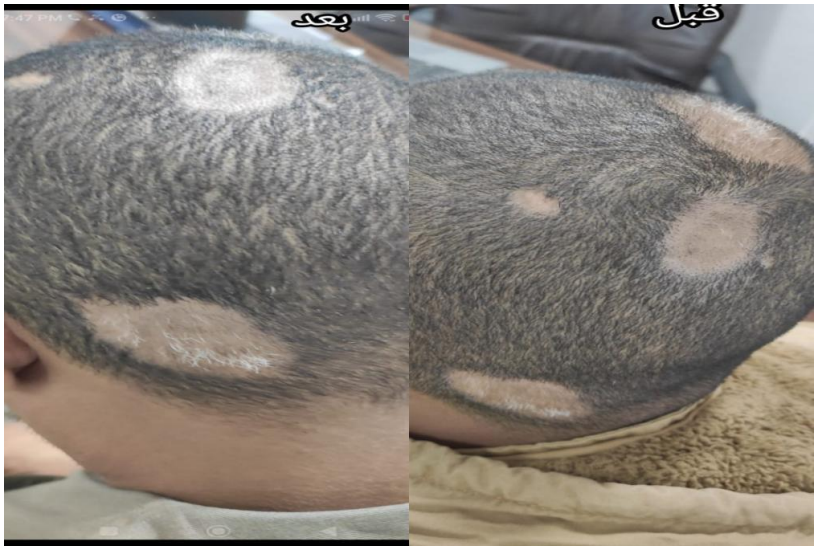

Figure 1: Picture of the patient's scalp before and after treatment

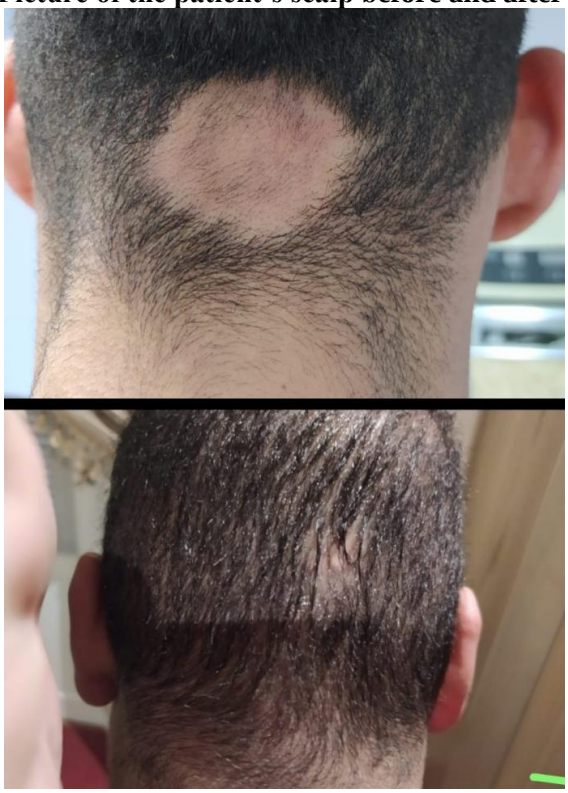

Figure 2: Picture of the patient's scalp before and after treatment

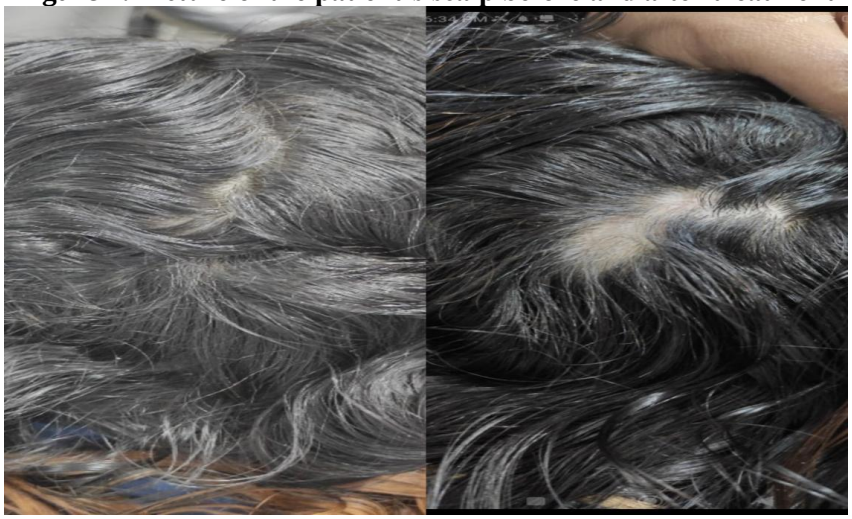

Figure 3: Picture of the patient's scalp before and after treatment

DISCUSSION

Intralesional TrA exerts its therapeutic effect primarily through suppression of the immune response, particularly by dampening the T-cell–mediated attack on hair follicles. Due to its comparatively lower risk of inducing cutaneous atrophy, TrA is widely regarded as the preferred corticosteroid for managing localized, patchy forms of AA [4].

In the present trial, changes in SALT scores clearly demonstrated the clinical benefit of both interventions. Mean scores declined substantially from baseline (MTX: 2.72 ± 1.49; TrA: 2.88 ± 1.45) to the three-month evaluation (MTX: 0.48 ± 1.42; TrA: 0.60 ± 1.41), reflecting marked improvement in both arms

These findings are consistent with those of **Rafique *et al.* [7],** who observed remission in 87.5% of patients treated with intralesional MTX and in 95.3% of those receiving intralesional TrA. The difference in remission rates between the two cohorts was not statistically significant.

Similarly, **Hamdino *et al.* [6]** reported no significant intergroup difference in SALT scores when assessed at baseline, after a 12-week treatment course, and again at three months post-therapy. Nevertheless, within-group comparisons revealed statistically significant reductions in SALT scores over time for both MTX and TrA recipients. At the end of the 12-week intervention, the TrA group exhibited a higher regrowth score compared with the MTX group, suggesting a possible early advantage for TrA despite overall comparable long-term outcomes.

Ganjoo and Thappa [8] reported that administering intralesional TrA at a concentration of 5 mg/mL every four weeks for 12 weeks resulted in complete hair regrowth in 47% of treated patients. In a comparable study, **Kuldeep *et al.* [9]** observed that using TrA at 10 mg/mL every three weeks for the same duration led to ≥75% regrowth in 60% of cases. Although our findings showed no statistically significant difference between MTX and TrA outcomes at the six-month assessment, the MTX group demonstrated a slight advantage in regrowth scores during the three-month follow-up period.

Similarly, **Srivastava *et al.* [10]** documented a gradual improvement in Regrowth Score (RGS) over time following intralesional TrA therapy, with RGS 4 achieved in 9% of patients by the fourth month, increasing to 40% by the fifth month, and reaching 60% by the sixth month. This sustained improvement was likely due to their extended treatment regimen, continuing TrA injections for up to six months at four-week intervals, in contrast to the shorter three-month protocol employed in our study.

In the series by **Kuldeep *et al.* [9]**, early response was also notable, with hair regrowth initiating as early as three weeks after starting intralesional TrA. Among their participants, the Healthcare Resource Group (HRG) IV subgroup achieved the best outcomes, with 60% (15 of 25) attaining substantial regrowth, followed by other treatment groups.

Abdelsalam *et al.* [11] investigated the role of intralesional MTX in localized AA and reported an overall response rate of approximately 93.3%. Notably, half of their patients (15 cases) achieved ≥75% hair regrowth. The regrowth scale scores recorded at the end of treatment were significantly higher compared with those observed at 4, 8, and 12 weeks of follow-up, indicating progressive improvement over time.

Regarding topical application, only a single published report has documented the successful use of MTX 1% gel as monotherapy in two patients with localized scalp AA **[12]**. By the end of the second month, both cases demonstrated the emergence of pigmented terminal hairs accompanied by mild scaling. The observed local reaction was mild, transient, and self-limiting, and was interpreted as potentially beneficial to the therapeutic process. The authors proposed that MTX may exert its effect in AA either through the induction of a localized irritant response, immunomodulatory activity, or a combination of both mechanisms.

In the current study, patient satisfaction was generally high in both treatment arms, with 64.0% of MTX recipients and 52.0% of TrA recipients reporting a high level of satisfaction. These results are consistent with satisfaction rates reported in comparable clinical trials. Nonetheless, a statistically significant difference in safety outcomes was observed ($p = 0.018$), with each therapy demonstrating a distinct adverse effect profile. Hyperpigmentation was more frequently encountered in the MTX group (32.0%), whereas hypopigmentation and dermal atrophy occurred exclusively in the TrA group (8.0% each).

Our findings differ from those of **Hamdino *et al.* [6],** who noted a higher—though statistically non-significant—satisfaction rate with MTX compared to TrA in adults with AA, and observed that all treatment-related adverse events were transient, resolving spontaneously during follow-up. Similarly, **Srivastava *et al.* [10]** reported that intralesional TrA was generally well tolerated, with telangiectasia developing in 7.5% of patients and atrophy in 4.6%, but no other substantial side effects.

In agreement with our results, no systemic adverse effects were recorded with intradermal MTX administration in other dermatologic conditions **[13]. Muhaidat *et al.*** [14] also reported minimal local adverse reactions to intralesional TrA, with skin shrinkage being the most frequently documented effect across different dosing regimens.

Conversely, **Balakrishnan *et al.* [15],** in a comparative study of intralesional PRP versus TrA for AA, found no adverse effects among TrA-treated patients, including no cases of cutaneous atrophy, pigmentary changes, telangiectasia, or burning sensations, which contrasts with our observations.

In the present trial, the mean number of treatment sessions was comparable between the two

groups, indicating a similar level of treatment efficiency. Both interventions produced noticeable clinical improvement by the 12-week assessment, suggesting that either approach can achieve relatively rapid results in appropriately selected patients. This contrasts with the findings of **Hamdino *et al.*** [6], who observed a slightly lower mean number of sessions in the MTX group compared with the TrA group, although the difference did not reach statistical significance.

Our results align more closely with those of **Rafique *et al.*** [7], who reported that patients in the MTX arm (Group A) had an average of 1.22 ± 0.42 lesions and required 3.30 ± 0.52 treatment sessions, while those in the triamcinolone arm (Group B) presented with an average of 1.20 ± 0.41 lesions and received 3.34 ± 0.48 sessions on average.

Based on our findings, intralesional MTX appears to be a safe and effective option for the management of patchy AA. Further research is warranted to explore the impact of varying MTX concentrations, different intervals between sessions, and its efficacy across diverse age groups, ideally involving larger patient cohorts to strengthen the evidence base.

This study has several limitations. The relatively small sample size and single-center design may limit the generalizability of the findings. The short follow-up period of six months may not fully capture long-term efficacy, relapse rates, or delayed adverse effects. Additionally, the use of a single concentration and fixed injection intervals for both MTX and TrA restricts conclusions regarding optimal dosing regimens. Objective assessment relied on the SALT score and photographic evaluation, which, although standardized, may be subject to observer bias. Future multicentre studies with larger cohorts, extended follow-up, and evaluation of varying dosages and injection protocols are warranted to validate and expand upon these results.

CONCLUSION

Our findings suggest that both MTX and TrA are effective treatments for localized AA, with similar efficacy but different safety profiles. The higher incidence of hyperpigmentation with MTX versus the risk of atrophy with TrA presents an important consideration for treatment selection, particularly in patients with different skin types or cosmetic concerns.

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