Dermatology Practical & Conceptual

Treatment Outcomes of Triamcinolone Acetonide Compared with Cryotherapy in Alopecia Areata: Evidence from a Systematic Review and Meta-Analysis

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Key words: Alopecia areata, Cryotherapy, Triamcinolone acetonide

Citation: Albarari SSA, Aisidat TAA, Musleh A, Edpuganti S. Treatment Outcomes of Triamcinolone Acetonide Compared with Cryotherapy in Alopecia Areata: Evidence from a Systematic Review and Meta-Analysis. *Dermatol Pract Concept*. 2026;16(1):6092. DOI: https://doi.org/10.5826/dpc.1601a6092

Accepted: August 24, 2025; **Published:** January 2026

Funding: None.

Competing Interests: None.

Authorship: All authors have contributed significantly to this publication.

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ABSTRACT

Introduction: Alopecia areata (AA) is a common autoimmune hair loss disorder. Intralesional triamcinolone acetonide (IL-TAC) and cryotherapy are both used for patchy AA, but their comparative efficacy and safety have not been systematically evaluated.

Objectives: The primary objective was to compare the efficacy of IL-TAC versus cryotherapy in achieving ≥50% hair regrowth in patchy AA. Secondary objectives included comparing safety profiles and conducting subgroup analyses.

Methods: We conducted a systematic review and meta-analysis per PRISMA 2020 guidelines (PROSPERO: CRD420251036356). Databases (PubMed, Scopus, CENTRAL, Google Scholar) were searched up to April 2025. Comparative studies of patients with patchy AA receiving IL-TAC or cryotherapy were included. Risk of bias was assessed using ROB2 and ROBINS-I tools. A random-effects meta-analysis was performed for the primary outcome.

Results: 640 patients across five trials were included. Sensitivity analysis of four studies demonstrated IL-TAC significantly increased the likelihood of ≥50% hair regrowth compared to cryotherapy (RR: 1.57; 95% CI: 1.36–1.81, *p*<0.001), with low heterogeneity (I^2=21%). Subgroup analyses by study design and randomization status found no significant differences. Adverse event profiles differed: IL-TAC was associated with injection-site pain and skin atrophy, while cryotherapy caused transient pain, swelling, and bullae.

Conclusions: Current evidence suggests IL-TAC is more effective than cryotherapy for significant hair regrowth in patchy AA, though both have distinct tolerability profiles. These findings support IL-TAC as a first-line procedural option, with cryotherapy remaining a viable alternative. Higher-quality comparative trials with standardized protocols and long-term follow-up are needed to confirm these findings.

Introduction

Alopecia areata (AA), the second most frequent non-scarring alopecia, is an immune-mediated disorder commonly affecting the scalp. It can progress to a total loss of scalp hair, known as alopecia totalis, or loss of body hair, known as alopecia universalis [1]. The prevalence of AA is estimated to be 2% worldwide, and it can affect individuals of any age at any point in time, but it most commonly begins at the age of 30 [2,3]. AA also has a significant impact on the patient's psychological well-being. Studies show that there is a prevalence of conditions like alexithymia, anxiety, and depression which impair the quality of life among the individuals who are affected [4].

The pathogenesis of AA involves the collapse of "immune privilege" in the hair follicle. This collapse triggers an autoimmune reaction leading to the destruction of the anagen hair follicles [5]. This is mediated mainly by CD8+ NKG2D+ T lymphocytes, interferon-gamma (IFN-γ), and interleukin-15 (IL-15), which contribute to the recruitment and activation of inflammatory cells around the anagen hair follicles. These cytokine-driven pathways result in the disruption of normal hair cycle and are linked closely to the activation of JAK/STAT signaling cascade [6].

Currently, there is no cure or evidence-based international treatment guidelines for systemic therapy for AA, and the treatment strategies vary widely depending on the severity and extent of hair loss. Therapeutic option includes topical agents like corticosteroids and minoxidil, intralesional corticosteroids, systemic immunosuppressants like methotrexate, cyclosporine, and emerging new therapies like JAK inhibitors. Physical therapies like phototherapy and cryotherapy are also used in some cases [7] Among these, intralesional corticosteroids, particularly triamcinolone acetonide (IL-TAC), are considered the first-line treatment for limited patchy AA due to their local efficacy and ease of administration and by functioning through local immunosuppression of the perifollicular inflammation. Common adverse effects include skin atrophy, telangiectasia, and hypopigmentation, particularly when used at a higher concentrations or when used over repeated sessions [8,9]. In contrast, cryotherapy involves the application of liquid nitrogen to induce localized tissue damage and inflammation, which is believed to modulate the autoimmune activity and stimulate the hair regrowth.

Cryotherapy is generally well tolerated, but its extreme cold can damage melanocytes and dermal structures. In particular, melanocytes are highly cold-sensitive, so scalp cryotherapy often produces pigmentary sequelae. Focal hypopigmentation or depigmented patches are well documented after cryosurgery, especially in darker skin types [10,11]. In practice, both hypo- and hyperpigmented macules commonly appear at treated sites [11,12]. More seriously, excessive freezing that penetrates the deep dermis can cause full-thickness cryo-burns. These deep burns disrupt the dermal basement membrane and adnexal structures (including hair follicles), often healing with permanent scar formation and alopecia [10,12]. In short, cryotherapy carries the well-recognized complications of post-inflammatory dyspigmentation and, if freeze depth is not strictly controlled, dermal burn-induced scarring [10,12].

Despite both IL-TAc and cryotherapy being utilized in the management of localized AA, there is a lack of head-to-head comparisons in the literature. Most available studies are limited by small sample sizes, inconsistent treatment protocols and heterogenous outcome measures, which complicate the evidence-based decision-making [13]. A systematic comparison of the safety and efficacy profiles of these two modalities is justified to direct clinical practice and maximize therapeutic results in patients with AA.

Objectives

Primary Objective

To systematically compare the efficacy of intralesional triamcinolone acetonide versus cryotherapy in achieving clinically significant hair regrowth (defined as ≥50% improvement) in patients with alopecia areata.

Secondary Objectives

1. To evaluate and compare the safety profiles of intralesional triamcinolone acetonide and cryotherapy.
2. To conduct subgroup analyses exploring potential effect modifiers, such as study design (split-scalp vs. parallel-group trials) and methodological quality (randomized vs. non-randomized studies).

Methodology

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines [14]. The study protocol was registered prospectively in the PROSPERO international systematic review registry (Registration number: CRD420251036356).

Literature Search

Comprehensive searches were performed across multiple electronic databases, including PubMed, Scopus, Cochrane Central Register of Controlled Trials (CENTRAL), and Google Scholar, with the final search conducted on 19 April 2025. The search strategy incorporated controlled vocabulary (MeSH terms) and free-text terms related to alopecia areata, intralesional steroids, and cryotherapy, with no date restriction applied. Detailed search strategies for each database are provided in File S1 and Figure S1. All identified records were imported into Rayyan systematic review software, where duplicate citations were removed prior to screening.

Participants

The study protocol was designed priorly with clearly defined eligibility criteria based on the PICO framework. We included comparative studies (randomized controlled trials and non-randomized clinical trials) that specifically evaluated patients of any age or sex with patchy alopecia areata, defined as localized hair loss with at least two patches, comparing triamcinolone acetonide at any concentration between 5 and 10 mg/mL against any form of cryotherapy (liquid nitrogen spray or contact) with a minimum follow-up period of three months. The primary outcome was the proportion of patients achieving ≥50% hair regrowth, while secondary outcomes included treatment-related adverse effects and patient satisfaction measures when reported. Studies were excluded if they were case reports or review articles.

Study Selection

The study selection process involved two independent reviewers, S.S.A.A. and T.A.A., who first screened titles and abstracts of all identified records, followed by full-text assessment of potentially eligible articles. Discrepancies at any stage were resolved through discussion or consultation with a third reviewer when necessary.

Data Collection Process

For included studies, two reviewers independently extracted data about study characteristics (design, setting, sample size), patient demographics, intervention details (including steroid concentration and cryotherapy protocols), outcome measures, and tolerability measures (adverse event reporting and patient dropout rates). When necessary, study authors were contacted to clarify missing or unclear data.

Risk of Bias Assessment

Risk of bias assessment was performed independently by two reviewers using the Cochrane Risk of Bias tool (ROB2) for randomized trials; ROBINS-I tool was used for non-randomized trials. Disagreements in risk of bias judgments were resolved through discussion. The visualization was done by Robvis tool for ROB2 and ROBINS-I [15,16].

It was inapplicable to measure the potential publication bias in our review by funnel plot since there were fewer than 10 included studies.

Data Synthesis

Meta-analysis of the primary outcome focused on comparing treatment efficacy by dichotomizing hair regrowth outcomes into clinically meaningful categories. We defined "good response" as ≥50% hair regrowth, combining reported moderate (50–75%) and excellent (>75%) response categories from included studies. This threshold was selected based on its established clinical relevance in alopecia areata treatment trials and consistency across most included studies. When studies used different percentage cutoffs, we mapped their original categories to our predefined ≥50% threshold through a multi-step process: initial independent categorization by two reviewers, followed by consensus discussions for discrepancies (with third reviewer when needed). This standardization, which involved the dichotomization and harmonization of varied outcome reporting, is a recognized and accepted practice in systematic reviews to ensure comparability and enable quantitative synthesis.

Treatment effects were expressed as risk ratios (RR) with 95% confidence intervals (CI), calculated using random-effects models to account for anticipated clinical heterogeneity. Otherwise, a fixed-effects model was used. The extent of statistical heterogeneity was quantified using I^2 statistics, with values exceeding 50% considered indicative of substantial heterogeneity.

Subgroup analyses examined potential effect modifiers, including study design split-scalp versus parallel-group and randomized versus non-randomized studies. Sensitivity analyses were conducted to assess the robustness of findings by excluding studies with high risk of bias or extreme effect. All statistical syntheses were conducted using RevMan 5.4, with additional qualitative synthesis of adverse event profiles and patient-reported outcomes when available.

Results

Description of Eligible Studies

The systematic search across multiple databases identified a total of 965 potential records, including seven from PubMed, 58 from Scopus, 11 from the Cochrane Library, and 889 from Google Scholar. After removing three duplicate records automatically through Rayyan, we screened 962 unique citations by title and abstract. This process yielded nine potentially eligible studies, which underwent full-text review. Ultimately, five studies, involving 640 patients, met our inclusion criteria and were included in the meta-analysis. The PRISMA flow diagram (Figure 1) visually summarizes this selection process.

Study Characteristics and Quality Assessment

The included studies were published between 2015 and 2025. Key characteristics, including study designs, participant demographics, assessment methods, severity of AA, intervention protocols, and outcome definitions, are summarized in Table 1.

All cryotherapy interventions used liquid nitrogen spray. Application protocols varied in freeze-thaw cycles (1–4) and session frequency (every 2–6 weeks).

Risk of bias was assessed for all included non-randomized studies using the ROBINS-I (Risk Of Bias In Non-Randomized Studies of Interventions) tool. All studies were judged to have moderate-to-serious risk of bias. ROB2 tool revealed some concerns across included randomized studies. The primary

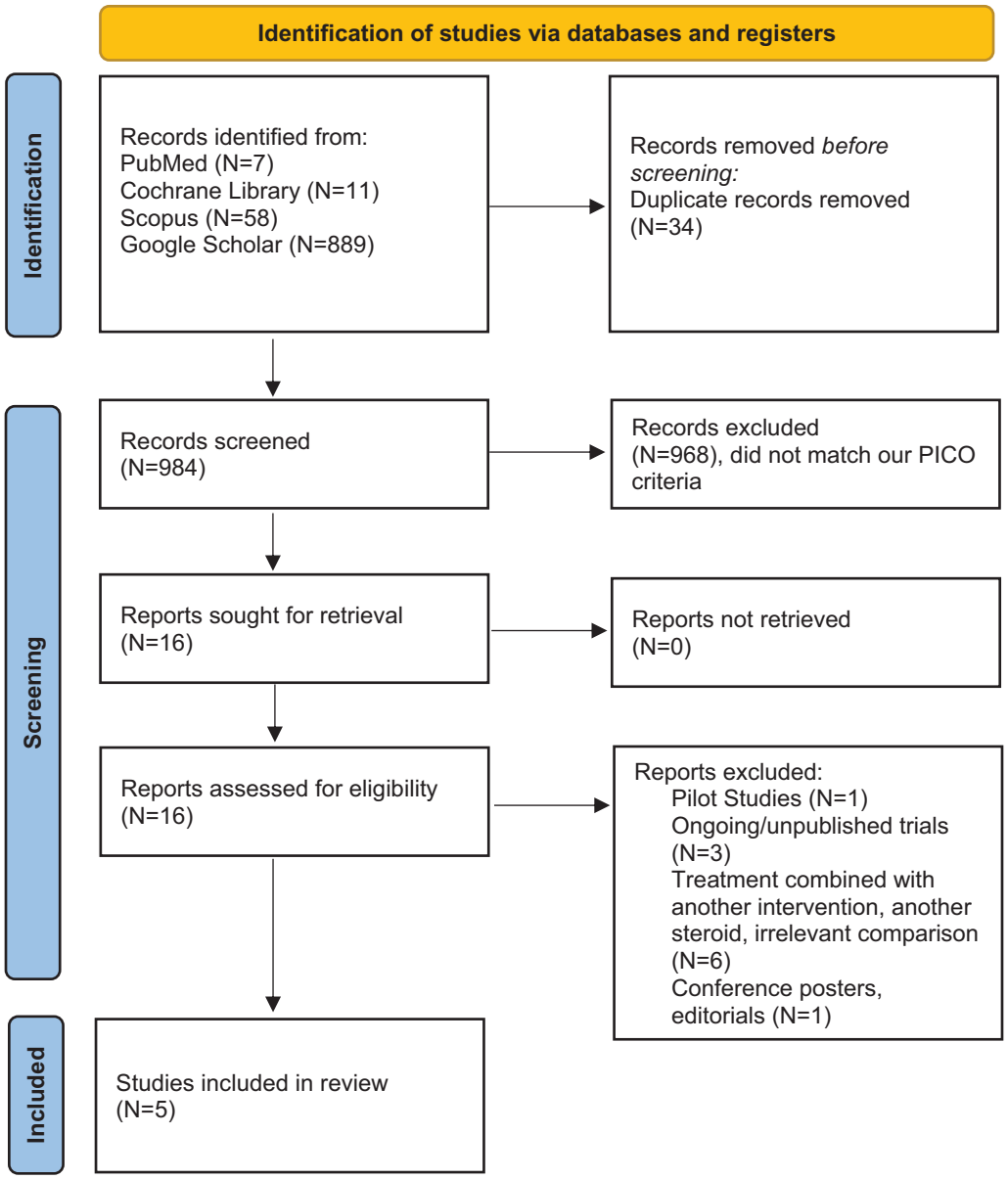


Figure 1. Identification of studies via database and registers.

Table 1. Characteristics of the included studies.

Study ID	Design	Participants N (TA vs Cryo)	Interventions (Dose/Frequency)	Assessment Method	AA Severity	≥50% Regrowth (TA vs Cryo)	Key Adverse Events (TA vs Cryo)	Patient Satisfaction
Mohammed et al. 2022 [17]	Split-scalp	30 pts (both groups)	TA: 5mg/mL q3wk ×4 Cryo: 2 cycles q3wk ×4	Clinical evaluation + dermoscope	Cryotherapy group: Median (IQR) SALT = 2.3% (1.8–4.8%) Steroid group: Median (IQR) SALT = 3.8% (2.4–6%).	60% vs 40%	NR	Median (IQR) on 5-point Likert scale: TA: 4 (3-5) Cryo: 4 (3-4)
Sayed et al. (2022) [18]	Split-scalp	21 pts (20 pts completed)	TA: 5mg/mL, monthly x4 Cryo: 3-4 cycles, q2wk x7	Trichoscopic assessment	Patients with patchy AA (at least 2 patches). SALT is not mentioned.	50% VS 45%	TA: Severe pain (5cases), atrophy/ telangiectasia (1, led to dropout) Cryo: None	NR
Sardana et al. (2022) [19]	Prospective comparative	50 pts (both groups)	TA: 10mg/mL, q4-6wk Cryo: 1 cycle, sessions NR	Clinical evaluation + SALT score	Cryotherapy group: Mean pre-treatment SALT = 0.59 ± 0.10. Steroid group: Mean pre-treatment SALT = 0.61 ± 0.08.	72% VS 54%	TA: Pain, transient atrophy Cryo: Pain, swelling, pruritus (more frequent)	Likert (mean -+SD): TA: 3.16-+ 0.84 Cryo: 2.54-+ 0.99
Ranjkesh et al. (2015) [20]	Analytical descriptive	120 pts (both groups)	TA: 5mg/mL, q3wk x4 Cryo: q3wk (cyclesNR)	Clinical evaluation	Matched for lesion location (80% scalp, 20% face), size, and duration. 83.3% of patients with disease duration <6 months.	83.4% VS 56.6%	TA: Pain (10%), atrophy (3.3%) Cryo: Bullae/ erythema (6.7%)	NR
Akram et al. (2025) [21]	Quasi-experimental	59 pts (both groups)	TA: 5mg/mL, q4wk x3 Cryo: q4wk x3 (cyclesNR)	Clinical evaluation	Steroid group: average size 6.31 ± 2.33 cm, duration 8.51 ± 3.94 months. Cryotherapy group: average size 6.89 ± 2.09 cm, duration 8.39 ± 3.13 months.	83.05% VS 50.85%	NR	NR

issues arose from inadequate reporting of randomization and allocation methods. The risk of bias summary is visually presented in (Figures 2–5).

Meta Analysis for Primary Outcomes

Three studies (Mohammed et al. 2022, Akram et al. 2025, Ranjkesh et al. 2015) explicitly reported ≥50% thresholds of hair growth, while two (Sayed et al. 2022, Sardana et al. 2022) required recategorization of their outcome data.

Although Sayed et al. [18] was included in the primary meta-analysis (Figure 6), due to extreme outlier effects (0% response in the TA arm), which violated model assumptions, we performed sensitivity analysis (Figure 7).

The sensitivity analysis confirmed that its exclusion both reduced heterogeneity (from 49% to 21%) and strengthened the association, as the relative risk increased from 1.54 to 1.57. This decision was justified by its clinically implausible null response rate (contradicting 60-98% TA efficacy in

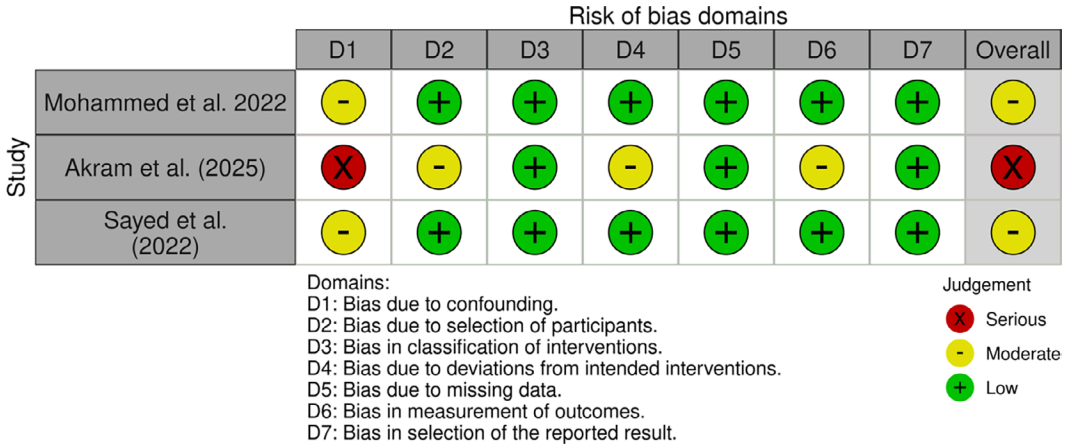


Figure 2. ROBINS-I of non-randomized trials: review authors' judgments about each domain for each included study.

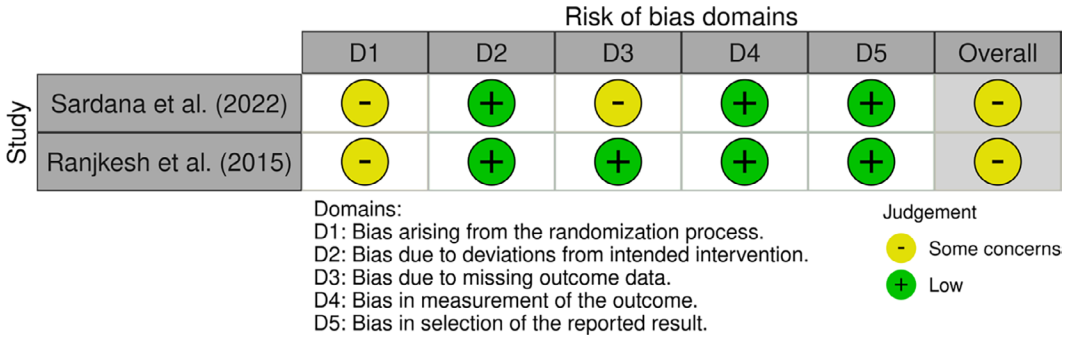
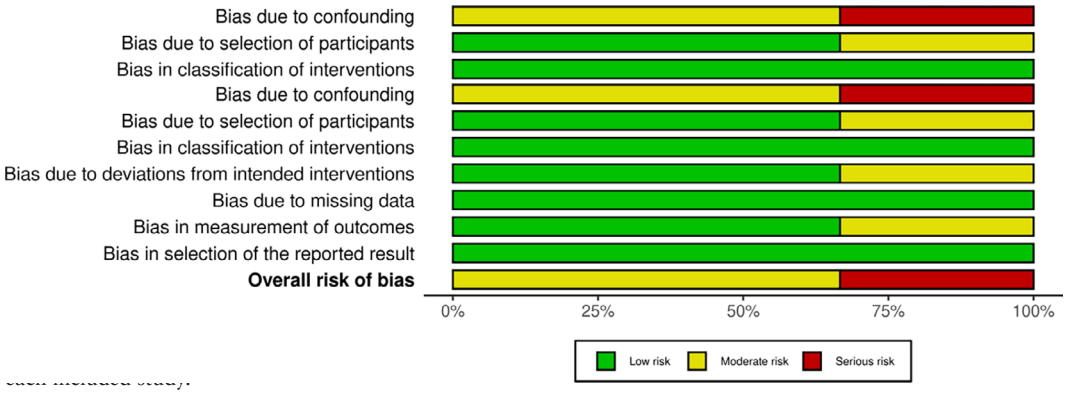


Figure 3. ROB2 of randomized trials: review authors' judgments about each domain for each included study.



each included study.

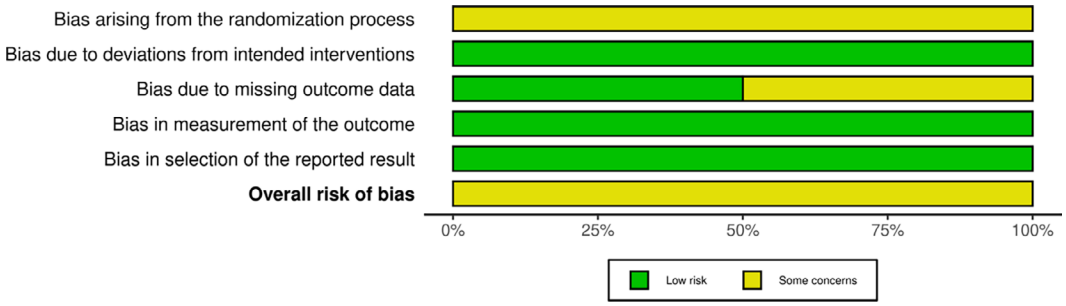


Figure 5. ROB2 of randomized trials summary graph: review authors' judgments about each domain for each included study.

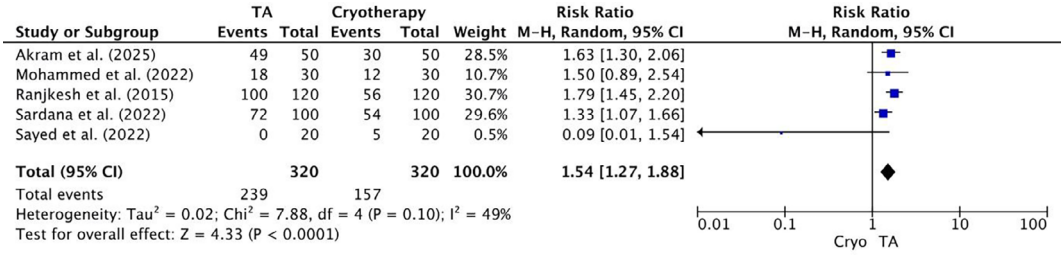


Figure 6. Forest plot of primary meta-analysis (all studies) for ≥50% hair regrowth.

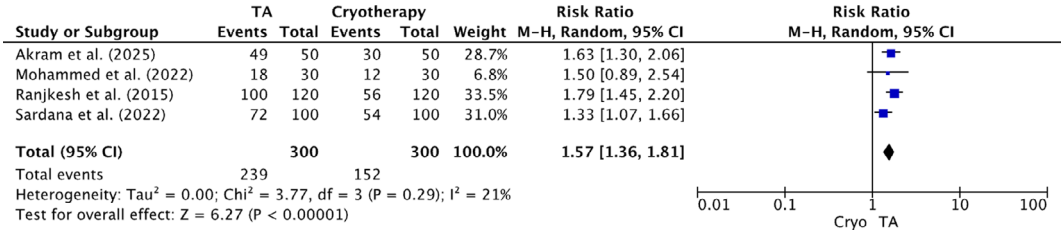


Figure 7. Forest plot of triamcinolone acetonide vs. cryotherapy efficacy (≥50% hair regrowth) (primary analysis, N=4 studies).

other studies), unblinded outcome assessment (high risk of bias), and improved model fit (I^2 <25% indicating low residual heterogeneity).

The sensitivity analysis of the primary outcome revealed that TA significantly increased the likelihood of achieving ≥50% hair regrowth compared to cryotherapy, with a risk ratio of 1.57 (95% CI: 1.36–1.81, P<0.001) and low heterogeneity (I^2=21%) (Figure 7). Subgroup analysis by study design showed no significant difference between split-scalp (RR=1.50, 95% CI: 0.89–2.54) and parallel-group (RR=1.58, 95% CI: 1.33–1.87) studies (P=0.86) (Figure 8). Another subgroup analysis was conducted to assess any difference in the results between randomized and non-randomized trials; the analysis showed no significant difference between randomized (RR=1.55, 95% CI: 1.16–2.06) and non-randomized (RR=1.61, 95% CI: 1.31–1.99) designs (P=0.82) (Figure 9).

Exploration of heterogeneity identified both clinical and methodological sources. Variations in steroid concentrations (5–10 mg/mL) and cryotherapy protocols (1–4 freeze-thaw cycles) represented key clinical differences, while variability in risk of bias across studies contributed to methodological heterogeneity. Assessment of reporting biases was limited by the small number of included studies, precluding meaningful funnel plot analysis.

Adverse Events

A qualitative synthesis of adverse events revealed different tolerability levels between treatments. For intralesional triamcinolone acetonide (IL-TAC), the most frequently reported complications included injection-site pain (10–25% of patients across studies) and localized atrophy (3.3–10%), with one case of telangiectasia leading to treatment discontinuation [18]. In contrast, cryotherapy was primarily associated with transient inflammatory reactions: pain and swelling were commonly described, while bullae and erythema occurred in 6.7% of patients in the Ranjkesh et al. (2015) study [20]. Notably, no instance of atrophy or long-term sequelae was documented with cryotherapy. The heterogeneity in adverse event reporting (variable definitions, inconsistent quantification) precluded formal meta-analysis, though the available data suggest IL-TAC carries higher risks

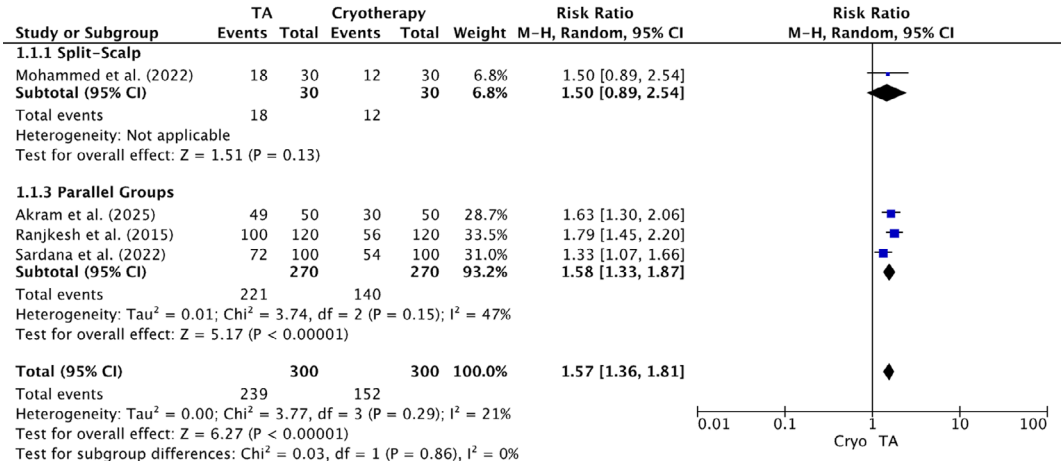


Figure 8. Forest plot of subgroup analysis (Split-Scalp vs Parallel Groups).

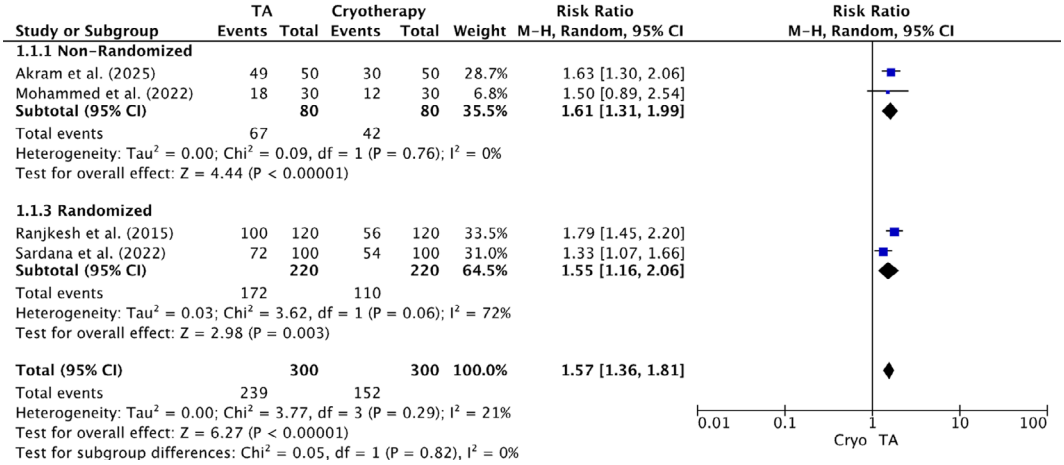


Figure 9. Forest plot of subgroup analysis (randomized vs non-randomized).

of persistent tissue changes, whereas cryotherapy's effects were typically acute and self-limiting.

Discussion

To our knowledge, this is the first systematic review and meta-analysis that compares intralesional triamcinolone acetonide and cryotherapy for patchy alopecia areata. It is crucial to contextualize our findings within the spectrum of alopecia areata severity. This meta-analysis specifically evaluated studies on patchy alopecia areata, where intralesional corticosteroids are often considered a first-line option. The results indicate an advantage of intralesional triamcinolone acetonide in achieving substantial hair regrowth within this specific patient group. While various therapeutic options are available for AA, and combination therapies are frequently employed in clinical practice, this review was designed to provide a head-to-head comparison of two widely used procedural monotherapies.

A pooled analysis of four studies found that intralesional triamcinolone acetonide was more effective than cryotherapy, with a 57% increase in the likelihood of achieving ≥50% hair growth. This robust effect size was maintained across subgroup analyses by study design and randomization status. While these preliminary results favor intralesional triamcinolone acetonide, the small number of studies (N=4) and their methodological limitations (bias risks, small samples) preclude definitive conclusions about superiority; clinicians should thus note that real-world outcomes may vary, as shown by Sayed et al.'s (2022) negative results [18]. Notably, the cryotherapy protocol in this study was unusually intensive (seven sessions with 3–4 cycles each), which may explain its relatively better performance compared to other studies using fewer cycles. This underscores the need for standardized administration protocols.

While our study focused on short-term hair regrowth, some evidence suggests cryotherapy might have potential advantages in relapse prevention, though this remains hypothetical due to limited long-term data in our analysis. Future studies should directly compare relapse rates between treatments. Kaiser et al. (2023) revealed that cryotherapy had lower relapse rates in some studies, but overall efficacy was

equivalent between the modalities. However, direct comparisons are limited by diversity in cryotherapy techniques (1–4 freeze-thaw cycles) among studies [22].

Despite the clinical significance of patient experience in alopecia areata (AA) management, only two included studies [17,19] assessed satisfaction metrics by using non-standardized Likert scales. This gap underscores the need for future trials to incorporate validated patient-reported outcome (PRO) measures such as the Alopecia Areata Symptom Impact Scale (AASIS) [23] or Dermatology Life Quality Index (DLQI) [24] to evaluate treatment-related pain, psychological burden, and quality of life. Standardized PROs would enhance shared decision-making, particularly when balancing efficacy against adverse effects (e.g., cryotherapy-induced pain vs. steroid atrophy).

Our finding that different concentrations were effective supports existing guidelines [25], though pilot data [26] suggest lower concentrations (2.5 mg/mL) may be equally effective while reducing atrophy risk The vascular effects of cryotherapy and disruption of inflammatory cascades may explain its more modest but potentially more sustained benefits [22].

The adverse effect (AE) profiles of IL-TAC and cryotherapy differed meaningfully. IL-TAC posed risks of local tissue damage (atrophy, telangiectasia), whereas cryotherapy primarily caused transient inflammation (pain, bullae). These findings suggest that cryotherapy may be preferable for patients at risk of steroid-related complications (e.g., those with thin skin), while IL-TAC remains a stronger option when rapid regrowth is prioritized.

The results of our study support intralesional triamcinolone acetonide as first-line for most patchy AA cases, particularly when rapid regrowth is prioritized. However, cryotherapy remains valuable for patients who have needle phobia [27], in resource-limited settings due to its lower cost and equipment needs [22], and in cases where steroid side effects (e.g., atrophy) are concerning, as two of our included studies showed [18,20].

Our study has significant limitations which future research should address. Variations in treatment methods, notably in terms of triamcinolone acetonide concentration and cryotherapy application techniques, contributed to clinical variability. The moderate-to-serious risk of bias in most included studies, owing primarily to insufficient randomization processes and outcome assessment blinding, further reduced methodological quality. While our qualitative synthesis revealed distinct AE profiles, the lack of standardized reporting precluded formal meta-analysis. We recommend that future trials adopt common AE criteria (e.g., CTCAE) to facilitate robust safety comparisons. All these limitations underscore the need for larger, more rigorously planned comparison trials with standardized methods and longer periods of follow-up to examine the long-term effectiveness of treatment.

The current evidence gap regarding long-term outcomes (>12 months) represents a critical area for future investigation, particularly given the chronic relapsing nature of alopecia areata. Comparative effectiveness studies of new treatments such as JAK inhibitors would help to contextualize these procedural alternatives in today's therapeutic landscape [28]. Additionally, research exploring optimized cryotherapy protocols (e.g., adjusted freeze times or intervals) may improve its efficacy while maintaining favorable safety profile. The possible synergistic effects of combining triamcinolone acetonide with adjuvant therapy such as minoxidil or microneedling have yet to be thoroughly investigated. To allow for cross-study comparisons, such studies should use standardized outcome measures that include both clinician-assessed and patient-reported endpoints.

Conclusion

Current evidence tentatively favors triamcinolone acetonide for limited patchy AA when rapid, robust hair regrowth is desired, but larger, higher-quality trials are needed to confirm these observations. While our study focused on monotherapies, future research should explore the role of combination regimens and optimal treatment strategies across the full spectrum of AA severity. Cryotherapy remains a valuable alternative for patients with contraindications to steroids or limited access to specialized care. Clinicians should engage in shared decision-making that balances efficacy expectations with individual risk tolerance and treatment accessibility. The efficacy of both approaches confirms their relevance in the treatment of alopecia areata. Future guidelines for treatment should consider this comparison as well as the need for further high-quality evidence to improve acceptable treatment regimens and patient selection criteria.

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