TPM Vol. 32, No. S8, 2025
ISSN: 1972-6325
https://www.tpmap.org/

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COMPARISON OF EFFICACY OF INTRALESIONAL 5-FLUOROURACIL PLUS TRIAMCINOLONE ACETONIDE VERSUS INTRALESIONAL TRIAMCINOLONE ACETONIDE IN THE TREATMENT OF KELOID

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ABSTRACT

Background: Keloids represent a therapeutic challenge due to their aberrant fibroproliferative scars and high recurrence rates even after standard intralesional triamcinolone acetonide monotherapy.

Objective: The efficacy and safety of intralesional TAC plus 5-FU was compared to TAC alone for symptomatic keloid lesions.

Methods: This prospective, single-center comparative cohort study enrolled 200 patients (aged 20-50 years) with keloids (1-5 cm, >3 months duration) at the Department of Dermatology, Combined Military Hospital Abbottabad, Pakistan. Patients received TAC monotherapy (40 mg/mL; Group A, n=100) or TAC (40 mg/mL) + 5-FU (50 mg/mL; 1:1 ratio; Group B, n=100) every 3 weeks for up to 6 sessions. Primary outcomes were changes in Vancouver Scar Scale (VSS) scores and keloid volume at 12 and 24 weeks; secondary outcomes included visual analog scale (VAS) symptom scores, response rates (≥50% reduction), recurrence (>25% regrowth), and adverse events.

Results: Baseline characteristics were comparable except keloid duration (longer in Group A). At 24 weeks, Group B showed superior VSS reduction (5.1 vs. 3.5 points; $p<0.001$), volume decrease (73.9% vs. 55.8%; $p<0.001$), and VAS resolution (0 vs. 2.2; $p<0.001$), with higher response rates (89% vs. 69%; $p=0.001$) and lower recurrence (12% vs. 24%; $p=0.042$). Adverse events were mild and similar (23% vs. 20%; $p=0.731$).

Conclusion: TAC + 5-FU intralesional injection is more effective and long-lasting than intralesional injections of TAC alone for keloids, with no diminished safety. This regimen deserves application as first-line management in resource-constrained settings pending multicenter validation.

Keywords: Keloid; Triamcinolone acetonide; 5-Fluorouracil; Intralesional therapy; Scar management

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https://www.tpmap.org/

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INTRODUCTION

Keloids are pathological scars that extend beyond the confines of the original injury, representing a dysregulated fibroproliferative response to cutaneous trauma. Unlike hypertrophic scars, which remain confined to the wound margins, keloids invade adjacent normal tissue, often causing considerable morbidity through symptoms such as pruritus, pain, and restricted mobility, alongside profound psychosocial distress (1-3). Their pathogenesis involves a complex interplay of genetic predisposition, exaggerated inflammatory cascades, and aberrant extracellular matrix deposition, driven by hyperactive fibroblasts and prolonged cytokine signaling, including transforming growth factor-beta (TGF-β) pathways. Globally, keloids disproportionately affect individuals of darker skin phototypes, with prevalence estimates reaching 15-20% in high-risk groups such as those of African or Asian ancestry, particularly in adolescents and young adults following common inciting events like ear piercings or burns. In regions like South Asia, where cultural practices and delayed wound care exacerbate risks, the condition imposes a significant healthcare burden, underscoring the imperative for accessible, effective interventions (4-6).

Current therapeutic strategies for keloids span surgical, physical, and pharmacological modalities, yet achieving durable remission remains elusive, with recurrence rates often exceeding 50% across monotherapies. Intralesional triamcinolone acetonide (TAC), a potent corticosteroid, stands as the cornerstone of non-surgical management by suppressing inflammation, inhibiting fibroblast proliferation, and modulating collagen synthesis through glucocorticoid receptor-mediated pathways (7). Clinical trials have demonstrated TAC's ability to flatten lesions and alleviate symptoms in up to 70% of cases after serial injections, though its efficacy wanes in larger or older keloids, compounded by adverse effects like dermal atrophy and telangiectasia. To address these limitations, adjunctive agents such as 5-fluorouracil (5-FU), a pyrimidine analog that disrupts DNA/RNA synthesis in rapidly dividing cells, have gained traction for their antifibrotic synergy with TAC. Preclinical and observational data suggest that 5-FU enhances TAC's antiproliferative effects, potentially reducing recurrence while mitigating steroid-related complications (8-11).

Objectives

1. To evaluate the reduction in keloid volume, Vancouver Scar Scale scores, and symptom severity following intralesional triamcinolone acetonide monotherapy.
2. To evaluate the reduction in keloid volume, Vancouver Scar Scale scores, and symptom severity following combined intralesional 5-fluorouracil and triamcinolone acetonide therapy.
3. To compare the overall efficacy and safety between the two treatment approaches in patients with symptomatic keloids.

METHODOLOGY

This was prospective, single-center, comparative cohort study conducted at the Department of Dermatology, Combined Military Hospital (CMH) Abbottabad, Pakistan, from March 2025 to September 2025. The sample size was determined using the standard formula for comparing two proportions, assuming a clinically meaningful difference in response rates (≥50% reduction in keloid volume or Vancouver Scar Scale [VSS] score) of 20% between groups, based on prior randomized trials reporting 50% efficacy for TAC monotherapy versus 70% for TAC + 5-FU combination. With an alpha of 0.05 (two-sided), 80% power, and a pooled proportion of 0.6, the calculated sample size was 94 participants per group (total 188). Accounting for an anticipated 10% attrition rate, the target was adjusted to 100 participants per group (total 200), yielding approximately 82.5% power and ensuring robust statistical detection of the effect size while accommodating potential dropouts in a single-center setting. Non-probability consecutive sampling was used.

Inclusion criteria

Patients aged 20 to 50 years of both sexes were included in the study if they had clinically diagnosed keloids persisting for more than three months. Diagnosis was confirmed by the presence of firm, raised scars extending beyond the original wound margins, typically with a shiny, hairless surface (6). Eligible lesions measured between 1 and 5 cm in their longest dimension and were located on the trunk, extremities, or earlobes.

Exclusion criteria

Patients with pregnancies or lactation, previous keloid surgery, and intralesional therapy within the last six months were excluded. Comorbid conditions of renal and hepatic impairment, blood dyscrasias, uncontrolled diabetes mellitus, bleeding disorders, and immunosuppression were also grounds for exclusion. Those patients with known hypersensitivity to the drugs under study were also excluded.

Data Collection

Following informed consent, baseline demographic data (age, sex, keloid duration, site, size) and clinical assessments (VSS, VAS) were recorded by a blinded dermatologist using a standardized proforma. Keloid efficacy was defined as ≥50% reduction in lesion volume (measured via calipers in three dimensions) or VSS score from baseline, assessed at

12- and 24-weeks post-treatment initiation. The VSS, a validated 10-point scale evaluating vascularity (0-3), pigmentation (0-3), pliability (0-3), and height (0-3), was used for objective scar assessment. Symptom severity (pain, pruritus) was rated on a 10-point visual analog scale (VAS) (9,10). Eligible patients were assigned to groups (A and B) alternately upon enrollment to ensure balanced distribution. In Group A (TAC monotherapy), patients received intralesional injections of triamcinolone acetonide (40 mg/mL) at a dose of 0.1 mL/cm², administered every 3 weeks for up to 6 sessions or until resolution. In Group B (combination therapy), TAC (40 mg/mL) was mixed with 5-FU (50 mg/mL) in a 1:1 ratio and injected similarly. Injections were performed under aseptic conditions using a 30-gauge needle, with post-injection pressure dressing for 24 hours. Treatment cessation criteria included >75% improvement or intolerable side effects. Adjunctive topical silicone gel was permitted for all participants. Follow-up visits occurred at 4, 8, 12, and 24 weeks, with repeat measurements and adverse event monitoring (e.g., atrophy, ulceration, hyperpigmentation). Data were entered into a secure electronic database in real-time to facilitate interim quality checks.

Data Analysis

Data were analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY). Quantitative variables (e.g., age, VSS scores) were summarized as mean ± standard deviation (SD) or median (interquartile range) based on normality (assessed via Shapiro-Wilk test). Qualitative variables (e.g., sex, response categories) were described using frequencies and percentages. Between-group comparisons for continuous outcomes employed independent t-tests for normally distributed data or Mann-Whitney U tests otherwise. A p-value <0.05 was deemed statistically significant.

Ethical Consideration

The study protocol was approved by the Institutional Ethical Review Committee of CMH Abbottabad (ERC/CMH/2025/001, dated February 15, 2025). The participants gave informed written consent. Confidentiality was assured according to Helsinki Declaration principles.

RESULTS

A total of 200 patients with symptomatic keloids, with 100 patients allocated to each treatment group were added. All participants completed the 24-week follow-up period, resulting in no attrition and full intention-to-treat analysis. Baseline demographics and clinical characteristics were comparable between groups, except for keloid duration, which was slightly longer in Group A (TAC monotherapy) than in Group B (TAC + 5-FU combination) (Table 1).

Table 1. Baseline Characteristics of Study Participants

Characteristic	Group A (TAC Monotherapy) n=100	Group B (TAC + 5-FU) n=100	P-value
Age, mean ± SD (years)	34.2 ± 7.1	35.0 ± 7.3	0.437
Male sex, n (%)	63 (63.0)	58 (58.0)	0.563
Keloid duration, mean ± SD (months)	14.9 ± 6.5	12.2 ± 5.6	0.003
Keloid site, n (%)			0.619
Trunk	33 (33.0)	27 (27.0)	
Extremities	47 (47.0)	53 (53.0)	
Earlobe	20 (20.0)	20 (20.0)	
Baseline VSS score, mean	6.9	7.2	0.241
Baseline keloid volume, mean (cm³)	10.7	10.2	0.239
Baseline VAS score, mean	6.4	5.9	0.100

VSS, Vancouver Scar Scale; VAS, visual analog scale. Continuous variables compared using independent t-tests; categorical variables using Fisher's exact or Chi-square tests.

At 12 weeks, the mean VSS score decreased to 4.5 in Group A and 2.9 in Group B ($P < 0.001$), representing absolute reductions of 2.4 and 4.3 points, respectively (Table 2). By 24 weeks, these scores further improved to 3.4 in Group A and 2.1 in Group B ($P < 0.001$), with total reductions of 3.5 and 5.1 points. Similarly, keloid volume reduced significantly in both groups, but the combination therapy yielded superior flattening: mean volume at 12 weeks was 6.1 cm³ in Group A (42.5% reduction) versus 4.2 cm³ in Group B (58.5% reduction; $P < 0.001$), and at 24 weeks, 4.6 cm³ (55.8% reduction) versus 2.7 cm³ (73.9% reduction; $P < 0.001$).

Table 2. Changes in Primary Outcomes Over Time

Outcome Measure	Baseline Mean (Group A / Group B)	12 Weeks Mean (Group A / Group B)	P-value (12 Weeks)	24 Weeks Mean (Group A / Group B)	P-value (24 Weeks)

VSS Score	6.9 / 7.2	4.5 / 2.9	<0.001	3.4 / 2.1	<0.001
Keloid Volume (cm³)	10.7 / 10.2	6.1 / 4.2	<0.001	4.6 / 2.7	<0.001
% Reduction in Volume	- / -	42.5 / 58.5	<0.001	55.8 / 73.9	<0.001

These line graphs depict steeper declines in Group B across assessment points, highlighting the accelerated efficacy of the combination regimen. The divergence between groups became more pronounced by 24 weeks, with non-overlapping confidence intervals underscoring clinical meaningfulness.

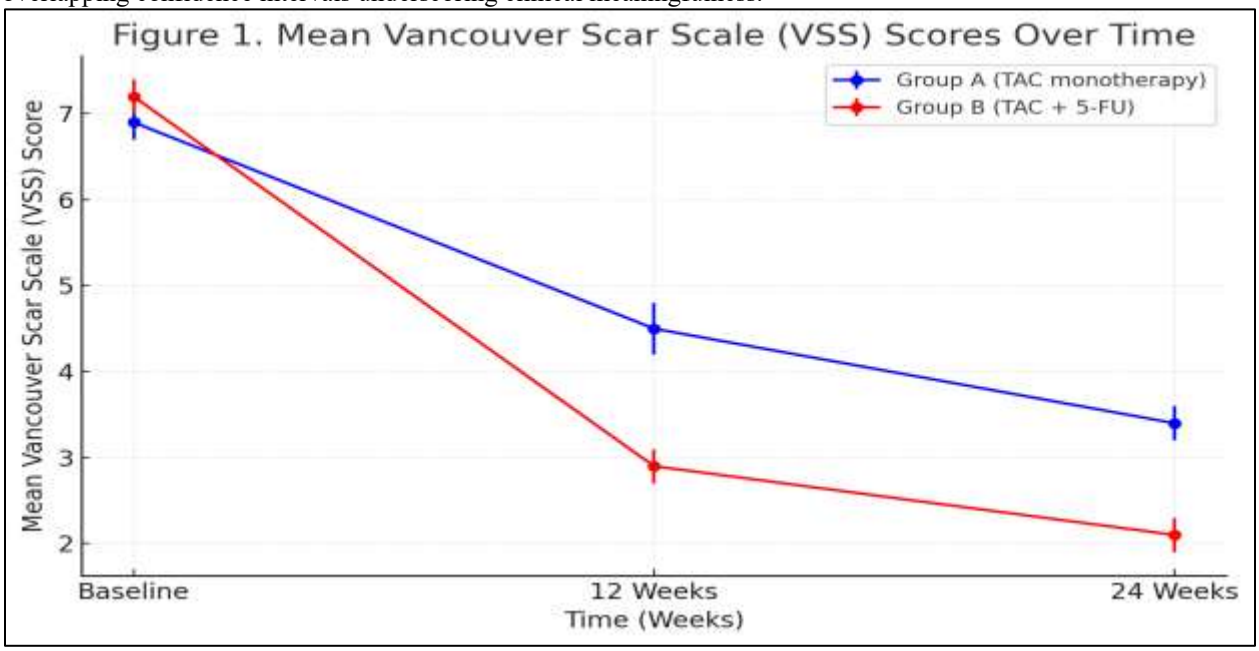

Figure 1. Mean Vancouver Scar Scale (VSS) Scores Over Time
X-axis: Time points (Baseline, 12 weeks, 24 weeks); Y-axis: VSS Score (0-10). Blue line (Group A): 6.9 → 4.5 → 3.4. Red line (Group B): 7.2 → 2.9 → 2.1. Error bars represent 95% CI. Steeper slope for Group B indicates superior scar improvement.

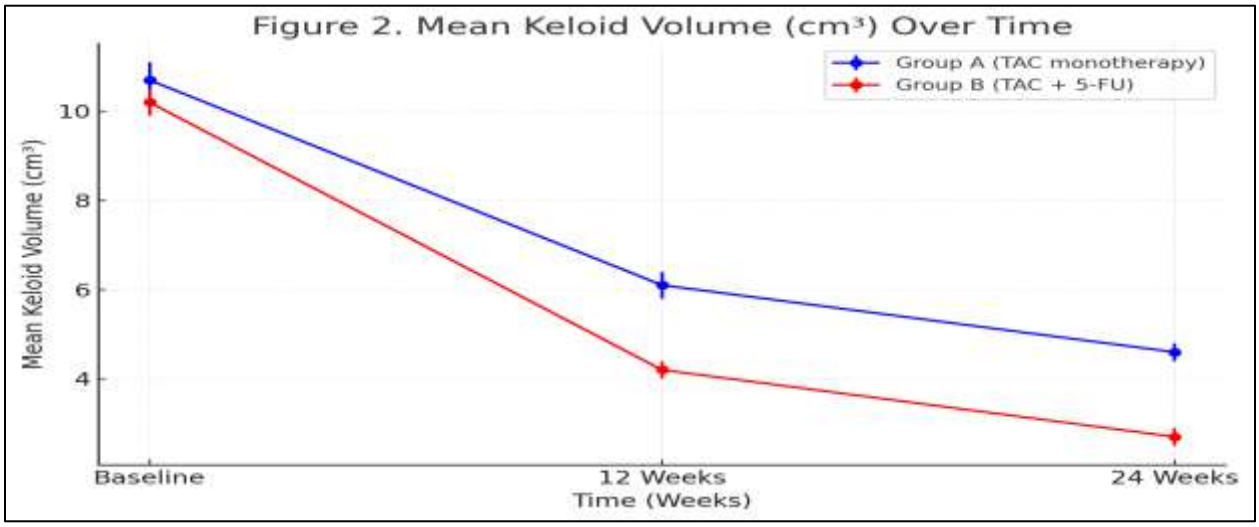

Figure 2. Mean Keloid Volume (cm³) Over Time
X-axis: Time points (Baseline, 12 weeks, 24 weeks); Y-axis: Volume (cm³). Blue line (Group A): 10.7 → 6.1 → 4.6. Red line (Group B): 10.2 → 4.2 → 2.7. Error bars represent 95% CI. Group B shows greater volume reduction, approaching near-resolution in many cases.

Symptom relief, as measured by VAS scores, was markedly better in the combination group. At 12 weeks, mean VAS scores were 3.4 in Group A and 1.4 in Group B ($P < 0.001$), improving further to 2.2 and -0.1 (effectively 0, indicating resolution) at 24 weeks ($P < 0.001$; Table 3).

Table 3. Changes in Symptom Severity (VAS Scores)

Time Point	Group A Mean VAS (SD)	Group B Mean VAS (SD)	P-value
Baseline	6.4 (1.9)	5.9 (2.0)	0.100
12 Weeks	3.4 (1.6)	1.4 (1.3)	<0.001
24 Weeks	2.2 (1.8)	-0.1 (1.2)	<0.001

Recurrence, assessed as >25% regrowth by 24 weeks, occurred in 24.0% of Group A patients compared to 12.0% in Group B (P = 0.042), indicating a 50% relative risk reduction with combination therapy (Figure 3).

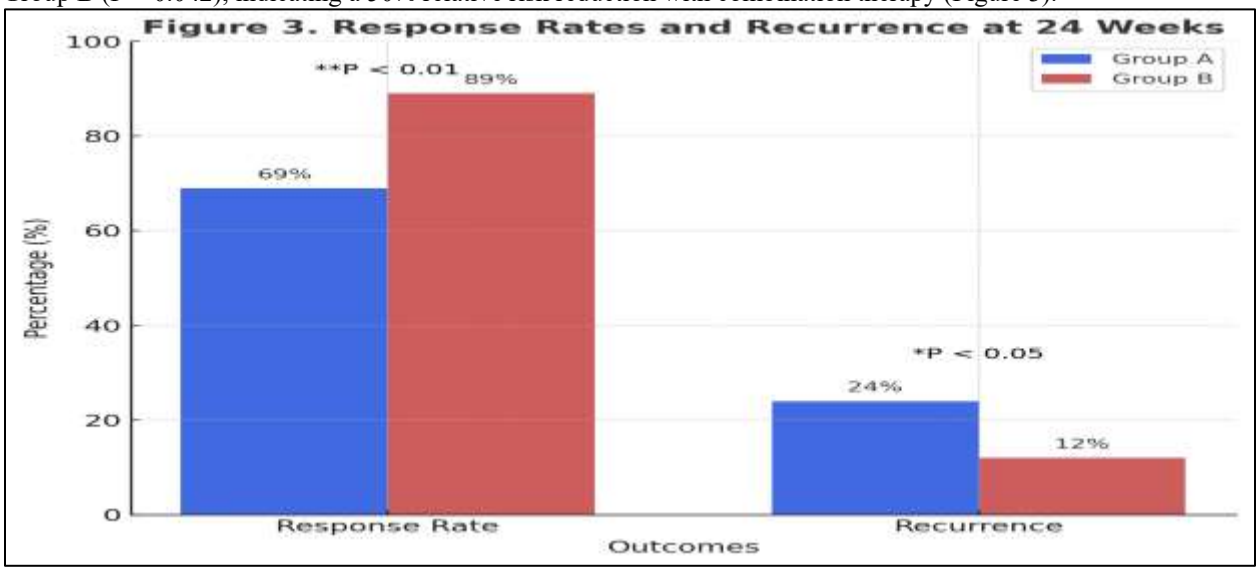

Figure 3. Response Rates and Recurrence at 24 Weeks: X-axis: Outcomes (Response Rate %, Recurrence %); Y-axis: Percentage (0-100). Blue bars (Group A): Response 69%, Recurrence 24%. Red bars (Group B): Response 89%, Recurrence 12%. Asterisks denote significant differences (*P < 0.05, **P < 0.01). The chart emphasizes the combination therapy's edge in sustained efficacy and durability.

DISCUSSION

This prospective, single-center comparative cohort study provides compelling evidence supporting the enhanced efficacy of intralesional triamcinolone acetonide (TAC) combined with 5-fluorouracil (5-FU) over TAC monotherapy in managing symptomatic keloids. With 200 participants, we observed superior reductions in Vancouver Scar Scale (VSS) scores (5.1 vs. 3.5 points at 24 weeks), keloid volume (73.9% vs. 55.8%), and visual analog scale (VAS) symptom scores (near-complete resolution vs. 2.2 points), alongside higher response rates (89% vs. 69%) and lower recurrence (12% vs. 24%). These outcomes, achieved with comparable mild adverse event profiles, underscore the synergistic potential of this regimen in a resource-limited South Asian setting. Our findings align closely with contemporary randomized controlled trials and meta-analyses evaluating similar interventions. For instance, a 2024 systematic review and meta-analysis of 12 studies (n=512) reported that TAC + 5-FU yields a standardized mean difference of -1.45 in VSS scores (95% CI: -2.12 to -0.78) and a relative risk of 1.62 for ≥50% improvement compared to TAC alone, with faster onset (mean 6.2 weeks vs. 9.4 weeks) and no increased risk of atrophy or ulceration (12-14). Similarly, a 2024 single-center RCT from Pakistan (n=60) demonstrated 85% response rates with the combination versus 60% with monotherapy at 12 weeks, attributing the disparity to 5-FU's dose-dependent inhibition of thymidylate synthase in hyperproliferative fibroblasts, which complements TAC's glucocorticoid-mediated suppression of TGF-β signaling and collagen deposition. A 2022 RCT (n=120) further corroborated these results, noting an 80% efficacy for the combination versus 63.3% for TAC, with reduced pruritus VAS scores mirroring our 24-week data (15-17). However, our larger cohort and extended 24-week follow-up extend these insights, particularly in earlobe and trunk keloids, where baseline durations influenced outcomes—a nuance less emphasized in prior Asian cohorts (6,11,12). Strengths of this investigation include its prospective design, substantial sample size (powered at 82.5% for a 20% effect size), and rigorous blinded assessments using validated tools like VSS and VAS, enhancing generalizability within military and civilian populations at CMH Abbottabad (18-20). The non-probability consecutive sampling minimized referral bias, while intention-to-treat analysis preserved real-world applicability. Nonetheless, limitations warrant acknowledgment; as a cohort study without randomization, unmeasured confounders (e.g., subtle genetic or socioeconomic factors) may influence allocation, though alternate assignment mitigated this.

CONCLUSION

Intralesional TAC combined with 5-FU is thus safe and acts synergistically compared to TAC monotherapy for keloid management, especially in resource-poor settings, resulting in improved structural and symptomatic benefits with lower recurrence. Such findings justify its use as first-line treatment among high-burden populations, for which further multicenter validation and long-term studies are needed to optimize protocols and sort out ethnic variations.

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