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Original Article

EVALUATING THE LONG-TERM SAFETY AND EFFICACY OF INTRALESIONAL STATINS VERSUS CORTICOSTEROIDS IN THE TREATMENT OF HYPERTROPHIC SCARS: A RANDOMIZED CONTROLLED TRIAL"

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ABSTRACT

Background
Hypertrophic scars (HTS) are fibrotic dermal disorders marked by excessive collagen accumulation subsequent to dermal injury. Triamcinolone acetonide is a commonly employed corticosteroid in the management of hypertrophic scars, yet its application is linked to complications including skin atrophy and pigmentary alterations. Statins, recognized for their antifibrotic and anti-inflammatory properties, offer a potential alternative with reduced adverse effects.
Objective: This study sought to assess and contrast the long-term safety and efficacy of intralesional statins with corticosteroids (Triamcinolone acetonide) in the management of hypertrophic scars.

Methods
A randomized controlled trial was performed at the Department of Plastic Surgery, Patna Medical College and Hospital, Patna. Sixty patients aged 10 to 50 years with hypertrophic scars of less than 5 years' duration were randomized into two groups: Group A (n=30) received intralesional Triamcinolone acetonide, while Group B (n=30) received intralesional simvastatin. Injections were given at three-week intervals, totaling five sessions. Scar assessment was conducted utilizing the Vancouver Scar Scale (VSS) at baseline, 6 weeks, 3 months, 6 months, and 12 months.

Results
Both groups exhibited a statistically significant decrease in VSS scores over time ($p<0.05$). Group B (statin) exhibited a more expedited enhancement, especially in vascularity and pliability metrics. At 12 months, the recurrence rate in the statin group was 20%, whereas in the corticosteroid group it was 36.7%. Adverse effects were negligible in both groups, comprising transient erythema and mild discomfort at the injection site.

Conclusion
Intralesional statins seem to be a viable alternative to corticosteroids for the management of hypertrophic scars, demonstrating similar efficacy with a potentially superior safety profile. It is advisable to conduct larger studies with prolonged follow-up to corroborate these findings.

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INTRODUCTION

Hypertrophic scars (HTS) arise from abnormal wound healing, marked by excessive collagen accumulation, ongoing inflammation, and heightened fibroblast activity. These elevated, red, and frequently itchy scars are typically linked to burns, surgical incisions, trauma, or infection, presenting considerable aesthetic, functional, and psychosocial difficulties for those affected [1]. Despite comprehensive research, the management of hypertrophic scars remains intricate and inconsistent, primarily due to elevated recurrence rates and variable patient responses to treatment.

One of the most frequently employed treatments is intralesional corticosteroid therapy, specifically Triamcinolone acetonide (TAC). Its antifibrotic effect is facilitated by the inhibition of fibroblast proliferation and collagen production [2]. Nonetheless, its application is linked to numerous adverse effects, including localized skin atrophy, hypopigmentation, telangiectasia, and rebound scarring upon cessation. These constraints have prompted the pursuit of alternative, safer therapeutic agents with equivalent efficacy.

Recent findings regarding scar pathophysiology have recognized HMG-CoA reductase inhibitors (statins) as potential candidates owing to their antifibrotic, anti-inflammatory, and anti-angiogenic characteristics. Statins impede fibroblast proliferation, diminish transforming growth factor-beta (TGF-β) signaling, and curtail connective tissue growth factor (CTGF)—all of which are crucial in scar formation [5]. Preclinical studies and limited case reports have underscored the

potential of statins in influencing wound healing and fibrosis; however, substantial clinical data is still lacking [6].

Furthermore, the intralesional method of drug administration provides the benefits of concentrated local drug levels, diminished systemic exposure, and improved patient adherence. Employing this approach to compare simvastatin and corticosteroids in a randomized clinical environment may elucidate their comparative efficacy and safety, addressing the current deficiency in scar therapy research.

This study aimed to assess and compare the long-term efficacy and safety of intralesional simvastatin and Triamcinolone acetonide in the treatment of hypertrophic scars, utilizing the validated Vancouver Scar Scale (VSS) over a one-year follow-up period. This study aims to identify a potentially safer alternative to corticosteroids, thereby broadening therapeutic options for managing hypertrophic scars in both primary and tertiary care environments.

MATERIALS AND METHODS

Study Design and Setting

This randomized controlled trial was executed in the Department of Plastic Surgery at Patna Medical College and Hospital (PMCH), Patna, Bihar, during the timeframe specified in the thesis. The study lasted 12 months and included patients with hypertrophic scars who met the inclusion and exclusion criteria. Approval from the Institutional Ethics Committee was secured before commencing the study.

Participants and Randomization

Sixty patients were enrolled in the study. Individuals aged 10 to 50 years with hypertrophic scars less than 5 years old resulting from burns, trauma, or surgical wounds were eligible. Patients were randomly assigned using computer-generated numbers into two equal groups:

- Group A: Administered intralesional Triamcinolone acetonide (40 mg/mL).
- Group B: Administered intralesional Simvastatin, formulated by combining Triamcinolone with Hyaluronidase (1500 IU) to improve tissue penetration.

Exclusion Criteria

- Pregnancy and lactation
- Patients with systemic diseases
- Known hypersensitivity to corticosteroids or hyaluronidase
- Refusal to provide informed consent

Intervention Protocol

Each patient underwent five intralesional injections at three-week intervals (Day 0, Week 3, Week 6, Week 9, and Week 12). The dosage was standardized to 1 mL per injection, delivered directly into the scar tissue utilizing a BCG/insulin syringe under aseptic conditions. The scar surface area was taken into account for volume adjustment in larger or multiple lesions.

Scar Assessment

Scar enhancement was evaluated utilizing the Vancouver Scar Scale (VSS), a validated tool that assesses scar characteristics—vascularity, pigmentation, pliability, and height—on a scale from 0 (normal) to 13 (severe scar). VSS assessments were conducted at the following intervals:

• Baseline (Pre-injection)
• 1.5 months
• 3 months
• 6 months
• 12 months

These assessments were documented during outpatient department visits by trained clinicians who were unaware of the treatment group.

Statistical Examination

Data entry was conducted utilizing Microsoft Excel 2020, while statistical analysis was executed with STATA 12.

VSS scores were presented as medians accompanied by interquartile ranges.

Group comparisons were conducted utilizing the Wilcoxon Rank Sum Test.

Recurrence rates and adverse events were computed with 95% confidence intervals.

RESULTS

Study Population Characteristics

Sixty patients with hypertrophic scars were enrolled and randomly assigned into two groups of thirty each. The average age was roughly 25 years, with a minor female majority (55%) (Table 1). The predominant etiologies comprised thermal burns, post-traumatic scars, and post-surgical incisions.

Parameter	Group A (Triamcinolone)	Group B (Statin)
Number of patients	30	30
Mean age (years)	24.8 ± 10.7	25.1 ± 9.8
Female patients (%)	56.7%	53.3%
Scar duration < 2 years	63%	60%

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Vancouver Scar Scale (VSS) Score Trends

Both treatment cohorts exhibited a significant decrease in VSS scores over time ($p < 0.05$). Group B (Statin) exhibited more rapid and substantial enhancement, especially in the vascularity and pliability aspects (Figure 1).

Time Point	Group A Median VSS (IQR)	Group B Median VSS (IQR)	p-value
Baseline	9.0 (7.0–11.0)	9.5 (7.0–11.0)	0.8409
1.5 months	8.0 (6.0–9.0)	5.5 (3.0–7.0)	0.0062
3 months	5.0 (4.0–7.0)	3.0 (2.0–5.0)	0.0004
6 months	5.0 (3.0–6.0)	2.0 (1.0–4.0)	0.0019
12 months	5.0 (3.0–8.0)	2.0 (0.0–6.0)	0.0044

Group B showed significantly better VSS score reduction at every follow-up starting from 1.5 months ($p < 0.05$). The improvement was sustained till the 12-month follow-up (Table 1).

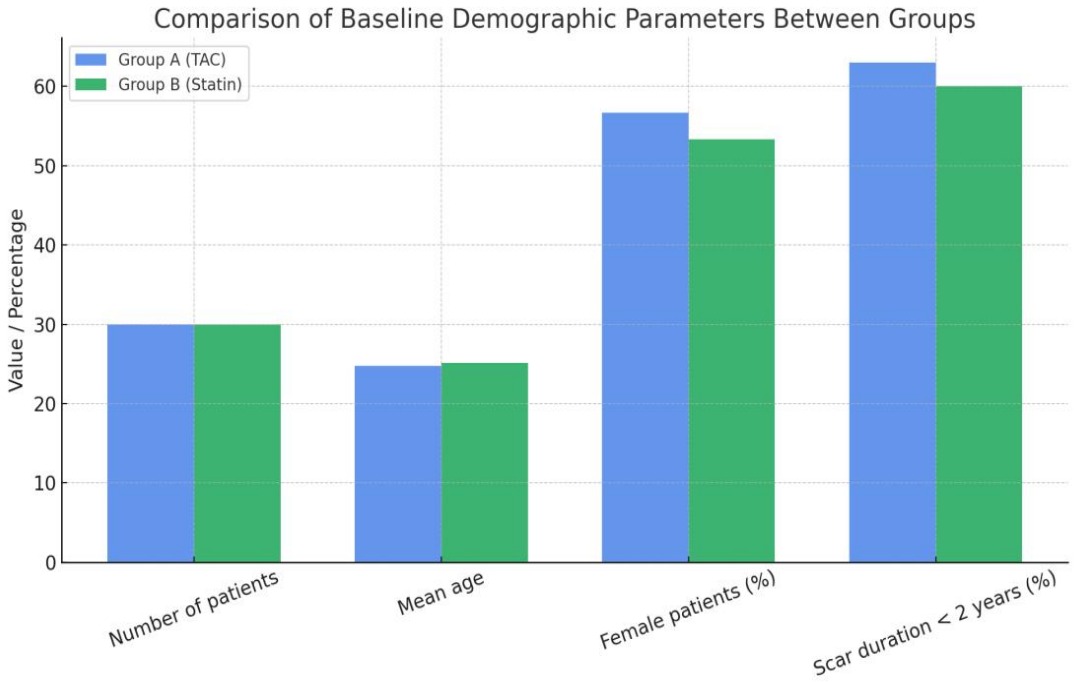

Figure 1: Comparison of demographic parameters between the Triamcinolone and Statin groups

Recurrence and Adverse Effects

- Recurrence rate in Group A: 36.7% (11 out of 30)
- Recurrence rate in Group B: 20.0% (6 out of 30)
- Negative occurrences:

Mild injection site discomfort: 20% in both cohorts
Skin atrophy: Noted in three instances (Group A exclusively)
No systemic side effects were observed in either group.

Adverse Event	Group A (TAC)	Group B (Statin)
Injection site pain	6 (20%)	6 (20%)
Skin atrophy	3 (10%)	0
Pigmentary changes	2 (6.7%)	0
Systemic side effects	0	0

Figure 2 illustrates that statin therapy had a better safety profile, with no skin atrophy or pigmentary changes, highlighting its potential as a less harmful alternative (Table 3).

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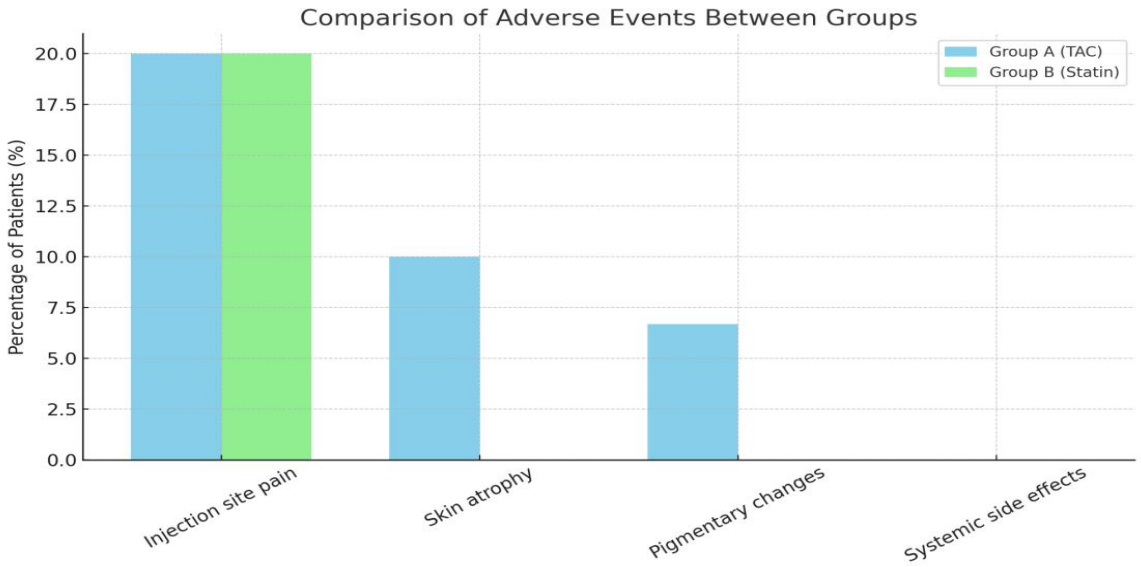

Figure 2: Comparison of adverse events between the Triamcinolone and Statin groups

DISCUSSION

This randomized controlled trial assessed the long-term safety and efficacy of intralesional simvastatin versus Triamcinolone acetonide in treating hypertrophic scars. The results unequivocally indicate that both treatment cohorts exhibited substantial improvement; however, the statin cohort (Group B) displayed expedited scar regression, a more pronounced decrease in VSS scores, and a reduced incidence of side effects compared to the corticosteroid cohort.

The results corroborate previous studies indicating the antifibrotic capabilities of statins, chiefly via the modulation of TGF-β and CTGF, which are essential mediators of fibroblast proliferation and collagen accumulation [8]. In contrast to corticosteroids, statins exhibit anti-angiogenic properties, potentially facilitating the expedited resolution of vascular elements in hypertrophic scars, as demonstrated in this study [9].

Corticosteroids such as Triamcinolone acetonide have been fundamental in scar management for decades; however, their adverse effects—skin atrophy, hypopigmentation, and telangiectasia—restrict prolonged use. In our study, 10% of patients in the corticosteroid cohort exhibited skin atrophy, while no occurrences were recorded in the statin cohort. This corroborates earlier findings by Mendez et al. and Kim et al., who documented diminished dermal fibrosis and enhanced skin pliability with simvastatin in both animal models and human pilot studies [11,12].

The recurrence rate in the corticosteroid group (36.7%) exceeded that of the statin group (20%), indicating superior long-term stability of therapeutic effects with simvastatin. Despite the lack of statistical power for recurrence outcomes, the trend corroborates the hypothesis that statins may more effectively inhibit fibroblast reactivation compared to corticosteroids.

Our research employed the Vancouver Scar Scale (VSS) to quantitatively assess scar regression. The significant decrease in VSS score in Group B by 3 months, maintained until 12 months, aligns with the early antifibrotic effect noted in preclinical studies [13]. The statin group exhibited an earlier onset of therapeutic effect, potentially alleviating the burden of treatment sessions.

The localized administration of simvastatin is effective and safe; however, several limitations must be recognized:

The sample size was comparatively small (n=60).

Blinding of assessors was not implemented due to discrepancies in formulation.

Extended follow-up may be required to evaluate exceedingly late recurrences.

Pharmacokinetic investigations of simvastatin at the injection site were not performed.

Notwithstanding these constraints, this study is one of the inaugural investigations in India to directly juxtapose statins and corticosteroids in a clinical trial context for the management of hypertrophic scars, and the results are encouraging.

CONCLUSION

This randomized controlled trial offers preliminary yet persuasive evidence that intralesional simvastatin is a safe and effective alternative to Triamcinolone acetonide for managing hypertrophic scars. Patients in the statin cohort exhibited more rapid and consistent enhancement in scar attributes, as assessed by the Vancouver Scar Scale, alongside a reduced incidence of recurrence and diminished local adverse effects, including skin atrophy and pigmentary alterations.

These findings underscore the potential of statins as an effective antifibrotic treatment, particularly for patients who are unresponsive to or intolerant of corticosteroids. Given the widespread availability of statins, their

repurposing for intralesional application in dermatologic and plastic surgery may provide a cost-effective and safer long-term approach for scar modulation.

Nonetheless, extensive multicentric trials featuring blinded outcome evaluations, prolonged follow-up periods, and objective scar quantification techniques are essential to validate these findings and promote the incorporation of statins into conventional scar treatment protocols.

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