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CLINICAL REPORT

Efficacy and safety of thermomechanical fractional injury-assisted corticosteroid delivery versus intralesional corticosteroid injection for the treatment of hypertrophic scars: A randomized split-scar trial

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Abstract

Background: Disruption of the natural skin barrier in a controlled manner may be used to deliver drugs that enhance scar resolution.

Objective: To compare the efficacy and safety of thermomechanical fractional injury (TMFI)-assisted topical corticosteroid delivery with corticosteroid injection in the treatment of hypertrophic scar (HTS).

Materials and Methods: This was a randomized, split-scar, double-blinded study. Twenty-one subjects with HTS on the abdomen received five split-scar treatments of TMFI + Steroid and steroid injection alone. Changes in scar thickness, scar volume, and Vancouver Scar Scale (VSS) were analyzed. Patient self-assessment, VAS scores, and adverse effects were also evaluated.

Results: Scar thickness, volume, and VSS scores of both segments improved significantly compared to baseline. On every follow-up visit, there were no significant differences in mean scar thickness reduction between the two treatment groups except at the 6-month follow-up where the mean scar thickness reduction of the steroid injection segment was significantly lower than that of the TMFI + Steroid segment (95% confidence interval [CI], 0.09–0.35; $p = 0.002$). Scar volume, VSS scores, and patient self-assessment also showed no significant differences between both segments on all visits. The steroid injection segment was significantly more painful than the TMFI + Steroid segment (95% CI, −2.16 to −1.29; $p < 0.001$). Adverse effects of skin atrophy, telangiectasia, and post-inflammatory hyperpigmentation were noted in the steroid injection segment, while no adverse effects were observed at the TMFI + Steroid segment.

Conclusions: TMFI-assisted topical corticosteroid delivery is an effective treatment for HTS with a lower risk of adverse effects compared with corticosteroid injection.

KEYWORDS

corticosteroids, drug delivery, hypertrophic scar, intralesional injection, keloid, thermomechanical fractional injury

INTRODUCTION

Hypertrophic scar (HTS) is a dermal fibroproliferative disorder that presents at sites of prior injury and wound repair. It is characterized by excessive deposition of collagen with altered morphology following local skin trauma or inflammatory skin disorders.[1,2] HTS may present with symptoms of pain, pruritus, and hyperesthesia.[3] These cause cosmetic disfigurement, and when present over mobile areas of the skin, may even cause contractions and limitations in joint mobility.[1]

Intralesional corticosteroid injection remains to be one of the most widely used first-line monotherapies for HTS.[3,4] Corticosteroids exert their effects on HTS via several mechanisms: (1) inflammatory response suppression, (2) vasoconstriction, (3) antimitotic inhibition of keratinocytes and fibroblasts causing slowed re-epithelialization and new collagen formation, and (4) downregulation of α-1-antitrypsin and α-2-macroglobulin inhibitors resulting in collagen degradation via increased collagenase activity.[5,6] The major drawback of corticosteroid injections is pain during administration, especially for pediatric patients and for those with large or multiple areas of involvement.[7] Other local side effects include bleeding at the injection site, infection of the injected skin areas, thinning and atrophy of the skin and subcutaneous tissue, development of steroid acne, telangiectasias, and hypopigmentation.[5,7]

Thermomechanical fractional injury (TMFI) facilitates the transcutaneous absorption of topical medications via the creation of micropores through the stratum corneum.[8–11] This relatively novel technique uses a heated (400°C) titanium medical grade tip comprising of 81 (9 × 9) pyramid-shaped micro-pins covering an area of 1 cm^2. The handpiece is placed vertically on the skin and when activated the tip travels at a preset speed and recedes in an automated fashion. The tip's apex comes into brief contact with the skin (6–18 milliseconds) to conduct heat, directly applying about 0.2 mJ/pyramid. At low settings, it creates an array of 81 fractional microscopic porous hemisphere-shaped thermal injury sites (200-μ deep and 300-μ wide) in which the stratum corneum layer is partially ablated. These sites exhibit enhanced permeability to hydrophilic topically applied substances. Permeability is facilitated by the humidity gradient that is formed between the skin surface and its underlying layers. The tip evaporates water during contact with the surface, with skin temperature decreasing relative to the distance between the tip (apex) and the affected tissue. Hence, water concentration within the tissue varies from very low concentration near the tip (low relative humidity) to that of normal skin water concentration at the base (high relative humidity), thereby providing an alternative pathway for drug flow into the skin.[10]

TMFI-assisted drug delivery has been shown by recent studies to overcome the local complications of intralesional injections while maintaining therapeutic concentrations of the drug at the target area.[12–15] The aim of this study is to compare the efficacy and safety of TMFI-assisted corticosteroid delivery with intralesional corticosteroid injection for the treatment of HTS.

METHODS

This was a prospective, randomized, split-scar, double-blinded comparative clinical study conducted between April 2020 and January 2021. The study was approved by the Siriraj Institutional Review Board, Faculty of Medicine, Siriraj Hospital, Mahidol University, Thailand (Si 719/2018) and was registered at ClinicalTrials.gov online registry (NCT04597060). Written informed consent was obtained from all subjects before treatment.

A total of 27 subjects with Fitzpatrick skin types (FST) III–IV with abdominal HTS resulting from surgery of at least 6 months' duration were enrolled. Subjects received a total of five treatment sessions given at 1-month intervals. Each scar was divided equally into two segments along its long axis to receive either "TMFI + Steroid" or "Steroid injection" only. Treatment assignment for each scar segment was generated using a block randomization plan from an online random block generator (www.randomization.com). Half of each scar assigned to the "TMFI + Steroid" treatment arm received TMFI (Tixel®; Novoxel® Ltd.) followed by immediate topical corticosteroid application using triamcinolone acetonide (TAC) suspension (40 mg/ml; 0.1 ml per 1 cm scar length) gently rubbed onto the scar for 2–3 minutes. A TMFI device (exposure time of 10 milliseconds; protrusion depth of 400 μm) was used to treat the designated scar section and a commercially available air-cooling machine (Cryo 6; Zimmer Aesthetics) was used to minimize pain and discomfort during the treatment. The "Steroid injection" segment was treated with intralesional TAC suspension (10 mg/ml) injection with a sufficient amount achieving complete blanching of the lesion. Only the treating physician (W.M.) was aware of the scar treatment assignment, while physician-observers involved in the preliminary and posttreatment assessment of the scars were blinded to the split-scar distribution.

Postoperatively, the scars were occluded under a transparent film dressing (Tegaderm™; 3M Health Care) left in place for at least 3 hours. No other post-procedural wound care instructions were given to the subjects.

CLINICAL ASSESSMENT

Objective and subjective evaluations regarding clinical improvement of the scars and adverse effects were obtained at baseline, then at 4-week intervals for a total of five sessions during the treatment phase, and during post-procedure follow-ups at 1-, 3-, and 6-month after the final (5th) treatment. All clinical photographs were taken with identical camera settings, lighting, and positioning. The objective evaluation included the measurement of HTS thickness using a dial caliper (Mitutoyo; Kanagawa, Japan), and scar volume using a skin imaging device (Antera® 3D CS; Miravex Limited). The means of three measurements of HTS thickness and scar volume for each subject were recorded. Systematic evaluation using the Vancouver Scar Scale (VSS)[16] was conducted by two treatment-blinded dermatologists.

This numerical scale ranging from 0 to 13 assesses four scar characteristics including vascularization, pliability, pigmentation, and height/thickness—the larger the number the worse the scar.

Patients were also asked to evaluate pain levels following the treatment for each segment using a visual analog scale (VAS), with the scale ranging from 0 (no pain) to 10 (severe pain). Recovery time and adverse effects and were also recorded at each treatment session and follow-up visit. During the final follow-up (6 months after the 5th treatment), patient self-assessment of overall scar improvement was done. The patients graded the improvement compared to a standardized photograph taken at baseline. Grading was done using percentages at 25% increments ranging from 0% (no improvement) to 100% (complete improvement).

Statistical analyses

Descriptive analysis was used for demographic data. Data were analyzed using a two-sided paired *t-test* with a confidence interval of 95% to assess the difference between the two treatment arms. Repeated measure analysis of variance (ANOVA) was used to compare differences between individual split-scars. Statistical analysis was performed using statistical software (IBM SPSS version 24.0; IBM) with $p < 0.05$ considered to be significant.

RESULTS

Patient demographic information is shown in Table 1. Twenty-one (18 females and 3 males) of the 27 subjects (77.8%) successfully completed the study protocol and were included in the final analysis. Six subjects withdrew from the study due to scheduling conflicts or were lost to follow-up. The mean age of the participants was 35.5 years (range, 22–54 years) and the majority had FST III (71.4%). The median scar duration was 3 years (range, 0.8–20 years).

HTS thickness

At baseline, there were no significant differences in the mean scar thickness between the two treatment groups (95% CI, −0.02 to 0.43; $p = 0.072$). In both TMFI + Steroid and steroid injection groups, mean scar thickness showed significant improvement when compared to baseline at all time points ($p < 0.001$) (Figure 1). On every follow-up visit, there were no significant differences in mean scar thickness reduction between the two treatment groups except at the 6-month follow-up where the mean scar thickness reduction of the steroid injection segment was significantly lower than that of the TMFI + Steroid segment (95% CI, 0.09–0.35; $p = 0.002$). Compared to baseline, the mean percentages of scar thickness reduction of the TMFI + Steroid segment were 56.7%, 60.5%, and 64.3% at 1-, 3-, and 6-months posttreatment, respectively, whereas the mean percentages of scar thickness reduction of the steroid injection segment were 46.9%, 65.0% and 74.2% at 1-, 3-, and 6-months posttreatment, respectively. Figure 2 shows the appearance of HTS in a representative patient at baseline and at 6 months after the final treatment.

Scar volume

At baseline, there were no significant differences in the mean scar volume between the two treatment segments

TABLE 1 Patient demographics

Characteristics	Value	*p* Value
Age, mean ± SD (min–max)	35.5 ± 7.96 years (22–54)	
Sex, *n* (%)		
Male	3 (14.3)	
Female	18 (85.7)	
Fitzpatrick skin type, *n* (%)		
III	15 (71.4)	
IV	6 (28.6)	
Duration of Scar, median (min–max)	3.0 years (0.8–20)	
Scar thickness by caliper, mean ± SD (min–max)	1.63 ± 0.83 mm (0.40–3.80)	0.072
TMFI + Steroid		
Steroid injection alone	1.43 ± 0.93 mm (0.10–4.10)	

Abbreviations: max, maximum; min, minimum.

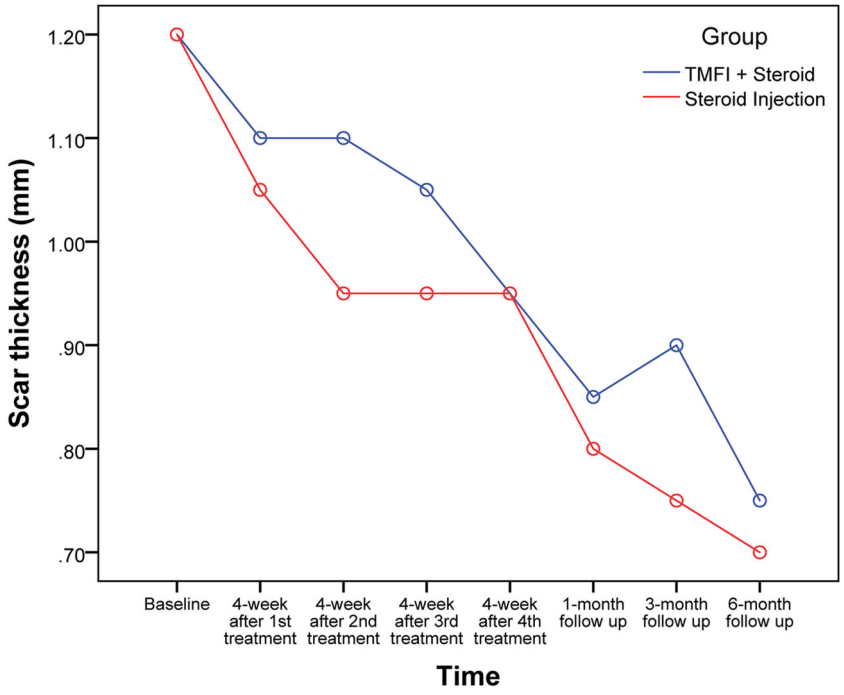

FIGURE 1 Mean scar thickness from baseline up to the 6-month follow-up visit

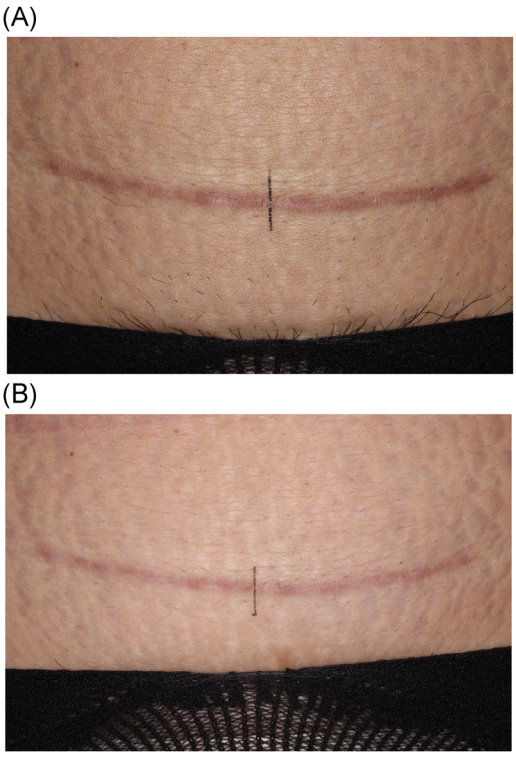

FIGURE 2 A 1-year duration hypertrophic scar in a 30-year-old patient with FST IV. The left half of the scar was treated with thermomechanical fractional Injury (TMFI) + steroid and the right half was treated with steroid injection. (A) Before treatment, (B) 6 months after five treatments

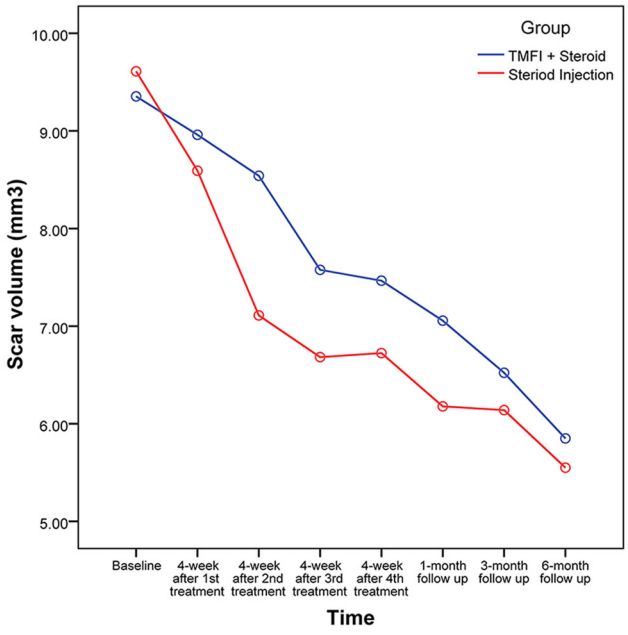

FIGURE 3 Mean scar volume from baseline up to the 6-month follow-up visit

(95% CI, −1.88 to 1.37; $p = 0.745$). In both TMFI + Steroid ($p = 0.014$) and steroid injection ($p = 0.001$) arms, the mean scar volume significantly decreased when compared to baseline at all time points (Figure 3). However, there were no significant differences in mean volume reduction from baseline when comparing the two interventional segments on every follow-up visit. The mean scar volume of the TMFI + Steroid segment decreased by 24.6%, 30.3%, and 37.5% from baseline, at 1-, 3-, and 6-month follow-ups, respectively, whereas the mean scar volume of the steroid injection segment decreased by 35.7%, 36.1%, and 42.3% from baseline, at 1, 3, and 6 months after the final treatment, respectively.

VSS

Before treatment, the VSS scores showed no significant differences between the two treatment segments (95% CI, −0.35 to 0.44; $p = 0.803$). The mean VSS scores of both the TMFI + Steroid and steroid injection branches showed significant improvement when compared to baseline at all time points ($p < 0.001$). At 6 months after the final treatment, the mean VSS of the TMFI + Steroid reduced from 6.61 ± 1.82 at baseline to 2.28 ± 1.70 (95% CI, 3.30–5.37; $p < 0.001$), whereas the mean VSS of the steroid injection segments decreased from 6.57 ± 2.11 at baseline to 2.52 ± 1.83 (95% CI, 2.49–5.61; $p < 0.001$). No significant differences in the mean VSS reduction between the TMFI + Steroid and steroid injection segments were present on each follow-up visit.

Patient self-assessment

At 6 months after the final treatment, 47.6% of the TMFI + Steroid group and 42.9% of the steroid injection group rated themselves as having more than 75% improvement from baseline. None of the patients reported 0% improvement. All patients preferred the overall treatment experience and outcome of the TMFI + Steroid segment compared to that of the steroid injection segment.

Recovery time, pain scores and adverse effects

Immediately after treatment, mild or moderate erythema and swelling lasting 3.12 ± 0.69 days were noted in all TMFI + Steroid segments. Bruise lasting 7.25 ± 0.69 was observed in 3 of 21 (14.2%) of the steroid injection segments. The mean VAS pain scores were 3.13 ± 1.84 and 4.79 ± 2.11 on the TMFI + Steroid with concomitant air cooling and steroid injection segments, respectively. The steroid injection segment was significantly more painful than the TMFI + Steroid segment with concomitant air cooling (95% CI, −2.16 to −1.29; $p < 0.001$). Adverse effects include skin atrophy (47.6%, 10/21 patients), telangiectasia (4.7%, 1/21), and post-inflammatory hyperpigmentation (9.5%, 2/21) which were noted in the steroid injection segments. No adverse effects were observed in the TMFI + Steroid segments on all follow-up visits.

DISCUSSION

The efficacy of a topical drug is correlated not only to its intrinsic potency but also to its ability to penetrate the layers of the skin, the principal barrier of which is the stratum corneum. Several modalities that alter or remove the stratum corneum have been used to facilitate the uptake of topical medications, including ablative fractional lasers, microdermabrasion, microneedling, sonophoresis, and radiofrequency, to name a few.[10,17,18]

As a means to enhance transdermal drug delivery, TMFI uses the transfer of thermal energy to create micropores on the skin. It combines a thermal effect of drying the skin and a motion effect of stretching the tissue in contact, leading to the formation of cracks that break through the stratum corneum. Due to the high temperature under the tip, it causes dehydration of tissue segments, creating a water concentration gradient allowing hydrophilic drugs to freely permeate through the gaps.[9–11] Pretreatment with TMFI has been demonstrated by previous studies to enhance transdermal drug delivery of several topical medications including verapamil, diclofenac, ascorbyl phosphate,[11] botulinum toxin type A,[14] and 5-amino-levulinic-acid hydrochloride (ALA).[10,15]

For this investigation, TMFI was followed by the topical application of TAC suspension. TAC suspensions contain triamcinolone acetonide, which is a lipophilic molecule in an aqueous solution. It is mainly intended for intralesional injection directly into the dermis for the treatment of HTS. Due to its lipophilicity, TAC suspension applied directly onto intact skin would be able to passively penetrate the stratum corneum as its molecular weight is <500 Daltons. This diffusion into the deeper layers of the skin is accelerated by the introduction of porous thermal injury sites from TMFI compared to the conventional intercellular route in between corneocytes.[10,19] Clinically, a blanching response was observed immediately after the TAC suspension was applied onto the HTS following TMFI, suggesting that the method facilitates cutaneous uptake of the suspension. The bioavailability of TAC in the skin following TMFI however, is beyond the scope of this investigation and should be explored further in future studies.

This study has shown that TMFI pretreatment before topical application of corticosteroids exhibits comparable therapeutic outcomes with intralesional corticosteroid injections for the treatment of HTS. Although the steroid injection arm exhibited a significant improvement in scar flattening over the TMFI + Steroid arm at 6-month follow-up (95% CI, 0.09–0.35; $p = 0.002$), the differences were not significant on any other follow-up visits. Furthermore, the scar volume and VSS scores did not demonstrate any significant differences between experimental groups on any follow-up assessment, showing comparable efficacies. Beyond its sufficient clinical effect, the other most notable benefit of TMFI pretreatment in combination with steroids is the significantly lower level of pain due to the procedure and the absence of any adverse events compared to intralesional corticosteroid injection. This makes this method of transdermal steroid delivery amenable for use in treating HTS in the pediatric population or in patients with large and/or multiple areas

of scarring. The additional cost of using TMFI, however, should be considered, as this method is more expensive than steroid injections alone.

A number of recent studies on the treatment of HTS have proven the adjunctive effect of TMFI with transcutaneous corticosteroid and/or 5-fluorouracil (5-FU) delivery. Artzi et al.[12] reported a significant reduction in the mean keloid VSS from 8.6 ± 1.2 to 5 ± 2.7 after eight TMFI-assisted TAC and 5-FU treatments in seven patients with recalcitrant keloid scars. The same investigator treated four children with hypertrophic burn scars and noted a statistically significant reduction in the mean scar VSS from 8.4 ± 0.8 to 5.2 ± 0.5 after eight treatments of TMFI combined with topical application of TAC 5-FU. Similarly, a lower pain score was reported with TMFI with a mean treatment pain VAS of 1.74 ± 0.9.[13] These findings are comparable to the treatment outcomes of our present study which shows a significant reduction in VSS from 6.61 ± 1.82 to 3.09 ± 1.57 during the 3rd month posttreatment follow-up, as well as a significantly lower pain score using TMFI. It should be noted, however, that the lower pain score of the TMFI + Steroid segment may be partly due to the concomitant air cooling during the treatment, whereas the steroid injection segment did not receive the same air cooling upon administration.

Ablative fractional lasers including Er:YAG and CO_2 lasers are means to provide deep transepidermal delivery of corticosteroids for the treatment of keloids and HTS. A study by Park et al.[20] conducted a prospective, split scar study on 10 Koreans with keloids on their left shoulder using an ablative fractional Er:YAG laser. Following laser treatment of the entire lesion, half of the scar received topical desoxymethasone 0.25% ointment, while the other half received intralesional triamcinolone acetonide (10 mg/ml) injections. Analogous to the findings of this study, the mean keloid VSS scores were significantly decreased from 8.59 ± 1.23 to 4.56 ± 1.09 on the laser and steroid injection side, and from 8.31 ± 2.09 to 5.02 ± 0.87 on the laser and topical steroid side after four treatments. There were no significant differences in VSS scores between the two treatment arms. Similarly, a retrospective study by Cavalie et al.[21] on 23 patients with 70 keloids that were resistant to first-line treatment showed 50% improvement in scar appearance after nine sessions of ablative fractional erbium laser treatment combined with topical betamethasone cream applied under occlusion twice daily. Another study done by Waibel et al.[22] using fractional CO_2 laser treatment combined with immediate postprocedure topical application of a TAC suspension (10–20 mg/ml) in 15 patients with HTS demonstrated an average overall improvement of 2.73 of HTS on a 0-3 scale. It is worth mentioning that for these other studies using ablative fractional lasers, the topical anesthetic was applied to the treatment area before the procedure, whereas no other anesthetic pretreatment was done for TMFI in this study apart from air-cooling during the procedure.

There are several limitations of the present study. First, the mean scar thickness of HTS is only 1.2 mm, thus, the outcome of this study may not necessarily represent the therapeutic response of thicker HTS. Second, it is generally difficult to demonstrate the appearance and improvement of HTS through two-dimensional photographs. Lastly, the design of this study cannot adequately dissociate the therapeutic effects of TMFI from the therapeutic agent, in this case, a corticosteroid. The repeated treatments of TMFI alone may sufficiently provide clinical improvement for hypetrophic scars as seen in studies on both non-ablative[23,24] and ablative[25,26] monotherapy fractional laser techniques for the treatment of HTS. Thermal energy delivered by fractional laser devices produces a controlled microwounding within the HTS, inducing wound remodeling leading to clinical improvement.[27] The remodeling process is hypothesized to be mediated by an increase in TGFβ3/type III collagen as seen in early wound healing and scarless fetal healing. However, a complex cascade of collagenases and the modulation of fibrotic pathways have complicated this picture.[28] A controlled prospective randomized study comparing TMFI alone and in combination with topical corticosteroid application will better evaluate this treatment technique and establish its superiority or inferiority. Another mandatory future study is to compare the TMFI versus laser-assisted corticosteroid delivery in the treatment of HTS.

CONCLUSIONS

All objective and patient-based assessments of the present study show that thermomechanical fractional injury-assisted topical corticosteroid delivery is a safe and effective treatment for hypertrophic scars with a lower risk of adverse effects and pain when used with concomitant air cooling compared with corticosteroid injections.

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CONFLICT OF INTERESTS

The authors declare that there are no conflicts of interest.

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REFERENCES

1. Berman B, Maderal A, Raphael B. Keloids and hypertrophic scars: pathophysiology, classification, and treatment. Dermatol Surg. 2017; 43(suppl 1):S3–S18. https://doi.org/10.1097/DSS.0000000000000819

2. Zhu Z, Ding J, Shankowsky HA, Tredget EE. The molecular mechanism of hypertrophic scar. J Cell Commun Signal. 2013; 7(4):239–52. https://doi.org/10.1007/s12079-013-0195-5
3. Wolfram D, Tzankov A, Pulzl P, Piza-Katzer H. Hypertrophic scars and keloids—a review of their pathophysiology, risk factors, and therapeutic management. Dermatol Surg. 2009;35(2):171–81. https://doi.org/10.1111/j.1524-4725.2008.34406.x
4. Hochman B, Locali RF, Matsuoka PK, Ferreira LM. Intralesional triamcinolone acetonide for keloid treatment: a systematic review. Aesthetic Plast Surg. 2008;32(4):705–9. https://doi.org/10.1007/s00266-008-9152-8
5. Morelli Coppola M, Salzillo R, Segreto F, Persichetti P. Triamcinolone acetonide intralesional injection for the treatment of keloid scars: patient selection and perspectives. Clin Cosmet Investig Dermatol. 2018;11:387–96. https://doi.org/10.2147/CCID.S133672
6. Sherris DA, Larrabee WF, Jr., Murakami CS. Management of scar contractures, hypertrophic scars, and keloids. Otolaryngol Clin North Am. 1995;28(5):1057–68.
7. Ogawa R. The most current algorithms for the treatment and prevention of hypertrophic scars and keloids. Plast Reconstr Surg. 2010; 125(2):557–68. https://doi.org/10.1097/PRS.0b013e3181c82dd5
8. Foged C, Haedersdal M, Bik L, Dierickx C, Phillipsen PA, Togsverd-Bo K. Thermo-mechanical fractional injury enhances skin surface- and epidermis-protoporphyrin IX fluorescence: comparison of 5-aminolevulinic acid in cream and gel vehicles. Lasers Surg Med. 2021; 53(5):622–9. https://doi.org/10.1002/lsm.23326
9. Kokolakis G, von Grawert L, Ulrich M, Lademann J, Zuberbier T, Hofmann MA. Wound healing process after thermomechanical skin ablation. Lasers Surg Med. 2020;52(8):730–4. https://doi.org/10.1002/lsm.23213
10. Shavit R, Dierickx C. A new method for percutaneous drug delivery by thermo-mechanical fractional injury. Lasers Surg Med. 2020;52(1):61–9. https://doi.org/10.1002/lsm.23125
11. Sintov AC, Hofmann MA. A novel thermo-mechanical system enhanced transdermal delivery of hydrophilic active agents by fractional ablation. Int J Pharm. 2016;511(2):821–30. https://doi.org/10.1016/j.ijpharm.2016.07.070
12. Artzi O, Koren A, Niv R, Mehrabi JN, Friedman O. The scar bane, without the pain: a new approach in the treatment of elevated scars: thermomechanical delivery of topical triamcinolone acetonide and 5-fluorouracil. Dermatol Ther (Heidelb). 2019;9(2): 321–6. https://doi.org/10.1007/s13555-019-0298-x
13. Artzi O, Koren A, Niv R, Mehrabi JN, Mashiah J, Friedman O. A new approach in the treatment of pediatric hypertrophic burn scars: Tixel-associated topical triamcinolone acetonide and 5-fluorouracil delivery. J Cosmet Dermatol. 2020;19(1):131–4. https://doi.org/10.1111/jocd.13192
14. Friedman O, Koren A, Niv R, Mehrabi JN, Artzi O. The toxic edge-A novel treatment for refractory erythema and flushing of rosacea. Lasers Surg Med. 2019;51(4):325–31. https://doi.org/10.1002/lsm.23023
15. Hilerowicz Y, Friedman O, Zur E, Ziv R, Koren A, Salameh F, et al. Thermomechanical ablation-assisted photodynamic therapy for the treatment of acne vulgaris. A retrospective chart review of 30 patients. Lasers Surg Med. 2020;52(10):966–70. https://doi.org/10.1002/lsm.23246
16. Thompson CM, Sood RF, Honari S, Carrougher GJ, Gibran NS. What score on the Vancouver Scar Scale constitutes a hypertrophic scar? Results from a survey of North American burn-care providers. Burns. 2015;41(7):1442–8. https://doi.org/10.1016/j.burns.2015.04.018
17. Haedersdal M, Erlendsson AM, Paasch U, Anderson RR. Translational medicine in the field of ablative fractional laser (AFXL)-assisted drug delivery: a critical review from basics to current clinical status. J Am Acad Dermatol. 2016;74(5): 981–1004. https://doi.org/10.1016/j.jaad.2015.12.008
18. Waibel JS, Rudnick A, Shagalov DR, Nicolazzo DM. Update of ablative fractionated lasers to enhance cutaneous topical drug delivery. Adv Ther. 2017;34(8):1840–9. https://doi.org/10.1007/s12325-017-0516-9
19. Jeong WY, Kwon M, Choi HE, Kim KS. Recent advances in transdermal drug delivery systems: a review. Biomater Res. 2021; 25(1):24. https://doi.org/10.1186/s40824-021-00226-6
20. Park JH, Chun JY, Lee JH. Laser-assisted topical corticosteroid delivery for the treatment of keloids. Lasers Med Sci. 2017;32(3): 601–8. https://doi.org/10.1007/s10103-017-2154-5
21. Cavalie M, Sillard L, Montaudie H, Bahadoran P, Lacour JP, Passeron T. Treatment of keloids with laser-assisted topical steroid delivery: a retrospective study of 23 cases. Dermatol Ther. 2015;28(2):74–8. https://doi.org/10.1111/dth.12187
22. Waibel JS, Wulkan AJ, Shumaker PR. Treatment of hypertrophic scars using laser and laser assisted corticosteroid delivery. Lasers Surg Med. 2013;45(3):135–40. https://doi.org/10.1002/lsm.22120
23. Lin JY, Warger WC, Izikson L, Anderson RR, Tannous Z. A prospective, randomized controlled trial on the efficacy of fractional photothermolysis on scar remodeling. Lasers Surg Med. 2011;43(4):265–72. https://doi.org/10.1002/lsm.21061
24. Niwa AB, Mello AP, Torezan LA, Osorio N. Fractional photothermolysis for the treatment of hypertrophic scars: clinical experience of eight cases. Dermatol Surg. 2009;35(5):773–7. https://doi.org/10.1111/j.1524-4725.2009.01127.x
25. Azzam OA, Bassiouny DA, El-Hawary MS, El Maadawi ZM, Sobhi RM, El-Mesidy MS. Treatment of hypertrophic scars and keloids by fractional carbon dioxide laser: a clinical, histological, and immunohistochemical study. Lasers Med Sci. 2016;31(1): 9–18. https://doi.org/10.1007/s10103-015-1824-4
26. Tawfic SO, El-Tawdy A, Shalaby S, Foad A, Shaker O, Sayed SS, et al. Evaluation of fractional CO2 versus long pulsed Nd:YAG lasers in treatment of hypertrophic scars and keloids: a randomized clinical trial. Lasers Surg Med. 2020;52(10):959–65. https://doi.org/10.1002/lsm.23249
27. Purschke M, Laubach HJ, Anderson RR, Manstein D. Thermal injury causes DNA damage and lethality in unheated surrounding cells: active thermal bystander effect. J Invest Dermatol. 2010; 130(1):86–92. https://doi.org/10.1038/jid.2009.205
28. Ozog DM, Liu A, Chaffins ML, Ormsby AH, Fincher EF, Chipps LK, et al. Evaluation of clinical results, histological architecture, and collagen expression following treatment of mature burn scars with a fractional carbon dioxide laser. JAMA Dermatol. 2013;149(1):50–7. https://doi.org/10.1001/2013.jamadermatol.668

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