Heliyon 9 (2023) e22818

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Treatment of hypertrophic scars with ablative fractional carbon dioxide laser assisted with different topical triamcinolone delivery ways

Junyi Zhou [1], Fen Hao [1], Ling Huang, Qingqing Fu, Lili Yuan, Gaoxing Luo, Jianglin Tan [*]

Institute of Burn Research, State Key Laboratory of Trauma, Burns and Combined Injury, Chongqing Key Laboratory for Disease Proteomics, Southwest Hospital, Army Medical University, Chongqing, 400038, China

ARTICLE INFO

Keywords:
Burn
Hypertrophic scar
Ablative fractional carbon dioxide laser
Triamcinolone

ABSTRACT

Objectives: Ablative fractional carbon dioxide laser has been used with triamcinolone to treat hypertrophic scars, resulting in promising success rates. However, there are different topical triamcinolone delivery methods used in scar treatment. To assess the efficacy among the different triamcinolone delivery methods, this study was designed to compare the efficacy and safety of ablative fractional carbon dioxide laser followed by penetration and injection of topical triamcinolone into thicker hypertrophic scars (height score of VSS $\geq$2).

Study design/materials and methods: We performed a retrospective study of 155 thicker hypertrophic scar patients (height score of VSS $\geq$2), including 88 patients in the triamcinolone external application group and 67 patients in the triamcinolone intralesional injection group. One month after the patients had 3 treatment sessions at 4-week intervals, the scars were assessed by photography, the Vancouver Scar Scale (VSS), durometry and spectrocolorimetry. Any adverse effects were also evaluated.

Results: The VSS scores and the hardness of the scars in both groups improved significantly compared to baseline. Moreover, the patients in the triamcinolone intralesional injection group had higher treatment efficacy (19.77 $\pm$ 21.25 %) based on their VSS scores than the patients in the triamcinolone external application group (5.94 $\pm$ 24.07 %), especially in the improvement of scar pliability, height and hardness. Meanwhile, in the triamcinolone injection group, more patients had mild and moderate improvement than in the triamcinolone application group. However, there were no differences in the distribution of the adverse effects in either group.

Conclusions: This study demonstrated that using the ablative fractional carbon dioxide laser followed by different topical triamcinolone delivery methods is effective and safe for thicker hypertrophic scar improvement. The method of using the ablative fractional carbon dioxide laser assisted with triamcinolone injection had a better therapeutic outcome in thicker hypertrophic scars, as compared with triamcinolone penetration.

* Corresponding author.
E-mail address: jianglintan@aliyun.com (J. Tan).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.heliyon.2023.e22818
Received 19 February 2023; Received in revised form 17 November 2023; Accepted 20 November 2023
Available online 23 November 2023

1. Introduction

Hypertrophic scarring is a pathognomonic feature characterized by excessive fibrosis with disordered collagens, leading to post-burn physical and psychosocial morbidity. The incidence rate of hypertrophic scars ranges from 30 % to 91 % following a burn injury [1]. The greatest unmet challenges in burn patients are related to the dysfunction and deformity from postburn scars [2]. The formation of hypertrophic scars is considered a result of an imbalance between extracellular matrix synthesis and degradation during wound healing [3]. The reduction of ECM synthesis and the promotion of ECM degradation can inhibit the formation of hypertrophic scars [4].

Laser treatment based on the theory of photothermolysis has been used to improve the appearance and function of scars [5]. Ablative fractional laser provides deep penetration and collagen remodeling, and dermal regeneration can be subsequently achieved. The optimized treatment depth should be proportional to the thickness of the scar. The depth of microscopic thermal zones (MTZs) induced by ablative fractional carbon dioxide laser is determined by the laser energy setting. To date, the maximal depth induced by an ablative fractional carbon dioxide laser is as high as approximately 4.0 mm in the dermis [6]. Therefore, obvious therapeutic effects cannot be obtained in thicker hypertrophic scars. Moreover, the incidence of adverse effects, such as bleeding, inflammation and infection, increases with increasing laser treatment energy. However, transdermal delivery followed by ablative fractional laser treatment could be better at improving scar formation [7]. Therefore, this study was designed to assess the efficacy and safety of ablative fractional carbon dioxide lasers assisted with different topical triamcinolone delivery methods for treating thicker hypertrophic scars (height score of VSS $\geq$2).

2. Results

1. Demographic characteristics of the patients.

A total of 155 patients, including 76 males and 79 females, were enrolled in this study. As shown in Table 1, 88 patients were enrolled with an average age of 29.7 years old (29.7 $\pm$ 11.4) in the triamcinolone external application group and 67 patients with an average age of 36.0 years old (36.0 $\pm$ 13.4) in the triamcinolone intralesional injection group. The scar height score was 2.86 $\pm$ 0.86 in the triamcinolone external application group and was 2.99 $\pm$ 0.77 in the triamcinolone intralesional injection group. The most common cause of injury in both groups was by fire/flame. The majority of the scars were located in the head and neck, followed by the upper limbs. A total of 48.4 % of the patients experienced scar pruritus, and 31.0 % suffered from scar pain. There were no significant differences in the distribution of sex, scar location, or adverse effects between the triamcinolone external application group and the triamcinolone intralesional injection group (Table 1).

2. Treatment efficacy after treatment

The overall VSS score of the patients in both the triamcinolone external application group and the triamcinolone intralesional injection group was significantly decreased. The VSS score results showed that scar pigmentation, vascularity, pliability and height was significantly decreased in the triamcinolone intralesional injection group, while only scar pigmentation was reduced in the triamcinolone external application group. The objective assessment results measured by durometry showed that the scar hardness in both groups was significantly decreased after the treatment compared to the pretreatment. However, the redness of the scar evaluated by

Table 1
Demographic and medical characteristics of the population.

Groups	triamcinolone external application	triamcinolone intralesional injection	P value	Total
Number of patients	88	67		155
Sex			0.307[a]	
Male, n (%)	40 (45.5 %)	36 (53.7 %)		76 (49.0 %)
Female, n (%)	48 (54.5 %)	31 (46.3 %)		79 (51.0 %)
Age at injury, (mean $\pm$ SD, years)	29.7 $\pm$ 11.4	36.0 $\pm$ 13.4		32.4 $\pm$ 12.6
Etiology, n (%)			0.000[a]	
Scald	20 (22.7 %)	7 (10.4 %)		27 (17.4 %)
Fire/Flame	35 (39.8 %)	40 (59.7 %)		75 (48.4 %)
Chemical agent	6 (6.8 %)	13 (19.4 %)		19 (12.3 %)
Electricity	6 (6.8 %)	4 (6.0 %)		10 (6.5 %)
Other	21 (23.9 %)	3 (4.5 %)		24 (15.5 %)
Scar location, n (%)			0.704[a]	
Head and neck	51 (58.0 %)	37 (55.2 %)		88 (56.8 %)
Trunk	5 (5.7 %)	7 (10.4 %)		12 (7.7 %)
Upper limbs	24 (27.3 %)	16 (23.9 %)		40 (28.4 %)
Lower limbs	8 (9.1 %)	7 (10.4 %)		15 (9.7 %)
Scar height score of VSS	2.86 $\pm$ 0.86	2.99 $\pm$ 0.77	0.204[b]	2.94 $\pm$ 0.82
Number of patients with scar pruritus, n (percent)	48 (54.5 %)	27 (40.3 %)		75 (48.4 %)
Number of patients with scar pain, n (percent)	21 (23.9 %)	27 (40.3 %)		48 (31.0 %)

Note. a: Chi-Square Test. B: ANOVA.

spectrocolorimetry did not significantly change in either group (Table 2).

3. Treatment efficacy between the triamcinolone external application group and the triamcinolone intralesional injection group

The patients in the triamcinolone intralesional injection group had a higher treatment efficacy (19.77 ± 21.25 %) based on the VSS score than the patients in the triamcinolone external application group (5.94 ± 24.07 %) (p = 0.000), especially in the improvement of scar pliability (20.52 ± 30.99 % vs. −2.56 ± 40.28 %) (p = 0.000) and height (18.78 ± 29.28 % vs. 0.40 ± 38.35 %) (p = 0.001). Meanwhile, the reduction percentage of scar hardness was much higher in the triamcinolone intralesional injection group (43.66 ± 34.65 %) than in the triamcinolone external application group (16.26 ± 43.84 %) (p = 0.000) (Table 3).

In the triamcinolone external application group, 4 (4.5 %) patients had significant improvement (50 % -≤ 75 %), 11 patients (12.5 %) had moderate improvement (25 % -≤ 50 %), 21 patients (23.9 %) had mild improvement (0 % -≤ 25 %), and 52 patients (59.1 %) had no improvement (≤0 %). Interestingly, in the triamcinolone intralesional injection group, more patients had mild (24 patients (35.8 %)) and moderate (23 patients (34.3 %)) improvement, and fewer patients had no improvement (16 patients (23.9 %)) (P = 0.000, Table 4).

4. The adverse effects between the triamcinolone external application group and the triamcinolone intralesional injection group

A total of 53.4 % of the patients in the triamcinolone external application group had adverse effects, including oozing (25.0 %), bleeding (15.9 %), and swelling (12.5 %), after laser treatment. In the triamcinolone intralesional injection group, 55.2 % of the patients had adverse effects, including oozing (29.9 %), bleeding (20.9 %), and swelling (4.5 %). However, there were no differences in the distribution of the adverse effects in either group. We did not observe atrophy or telangiectasia in either group (P = 0.172, Table 5).

3. Discussion

Hypertrophic scarring is the result of abnormal wound healing, presenting as continuous inflammation, fibroblast proliferation, vascularization and collagen deposition [8]. Over the past few decades, laser treatments have been demonstrated to play a fantastic role in the improvement of multiple scar characteristics, including thickness, color, pruritus, and pain [9]. Ablative fractional carbon dioxide lasers have been used widely in the management of different scars, especially hypertrophic scars. The mechanism of ablative fractional carbon dioxide laser serves to restore the collagen architecture and inhibit transforming growth factor β1 expression, resulting in increases in the dermal pliability, reduction in the thickness and promotion of a mature scar.

Corticosteroid injection, alone or combined with other therapeutic procedures, is a mainstay in the treatment of hypertrophic scars [10]. Recent meta-analyses have shown that intralesional corticosteroids can induce regression in 50 %–100 % of cases and that there is a 9 %–50 % recurrence of hypertrophic scars [11–13]. Corticosteroids modulate the wound healing process by decreasing fibroblast proliferation, inflammatory cytokine production, and collagen and glycosaminoglycan synthesis, resulting in suppression of the synthesis of inflammatory mediators, such as transforming growth factor β1 (TGF-β1). However, the application of corticosteroid injections are always used in small and/or single scar areas. The adverse effects of corticosteroid injections are pain, skin atrophy, hypopigmentation, hyperpigmentation, and telangiectasia [14].

Manuskiatti reported that thermomechanical fractional injury-assisted topical corticosteroid delivery is an effective treatment for hypertrophic scars with a lower risk of adverse effects [15]. However, the mean scar thickness in this study was only 1.2 mm, which cannot completely represent the therapeutic response of hypertrophic scars, especially scars more than 2 mm in height. In our study, we studied thicker scars (≥2 height of VSS) and demonstrated improvement when using laser combined with both topical triamcinolone delivery methods. We found that the VSS and hardness score were decreased after treatment in both groups. The ablative fractional carbon dioxide laser used in our study was set to the deep mode with an energy range of 30 MJ, which was correlated with a treatment depth of 800 μm. This maximum treatment depth was less than the thickness of the scar. However, using the ablative fractional carbon dioxide laser followed by triamcinolone delivery could also improve hypertrophic scar formation. After ablative fractional laser treatment, the laser channel in the skin showed an 'empty' zone, which can enhance drug penetration and absorption [16,17]. In addition, Emily et al. found uniform dermal drug distribution in the ~520 μm lateral spaces between laser channels [18].

Table 2
Assessment results before (pre-) and after (post-) treatment.

Hypertrophic scar	triamcinolone external application			triamcinolone intralesional injection		
	Pre-treatment (M±SD)	Post-treatment (M±SD)	p-value	Pre-treatment (M±SD)	Post-treatment (M±SD)	p-value
VSS	8.73 ± 1.81	8.08 ± 2.19	0.034*	9.75 ± 1.54	7.84 ± 1.94	0.000**
Pigmentation	1.89 ± 0.60	1.67 ± 0.69	0.028*	2.10 ± 0.46	1.82 ± 0.42	0.000**
Vascularity	1.72 ± 0.66	1.52 ± 0.71	0.063	1.97 ± 0.43	1.57 ± 0.53	0.000**
Pliability	2.26 ± 0.67	2.18 ± 0.70	0.443	2.69 ± 0.66	2.09 ± 0.67	0.000**
Height	2.86 ± 0.86	2.70 ± 0.91	0.235	2.99 ± 0.77	2.36 ± 0.79	0.000**
hardness	25.70 ± 14.65	18.41 ± 9.45	0.000**	26.87 ± 13.09	13.62 ± 9.24	0.000**
lightness	47.44 ± 5.14	49.30 ± 4.96	0.016*	47.25 ± 4.42	48.69 ± 5.10	0.083
Redness	10.14 ± 2.66	9.57 ± 2.46	0.141	9.98 ± 2.67	9.63 ± 2.35	0.421

Note. M = mean; SD = standard deviation. Paired-Sample t-tests.

Table 3
Treatment efficacy between the two groups.

Hypertrophic scar	triamcinolone external application (M±SD)	triamcinolone intralesional injection (M±SD)	p-value
VSS%	5.94 ± 24.07	19.77 ± 21.25	0.000
Pigmentation%	9.28 ± 34.36	10.70 ± 26.70	0.781
Vascularity%	11.74 ± 34.29	16.67 ± 39.36	0.407
Pliability%	−2.56 ± 40.28	20.52 ± 30.99	0.000
Height%	0.40 ± 38.35	18.78 ± 29.28	0.001
Hardness%	16.26 ± 43.84	43.66 ± 34.65	0.000
Lightness%	−4.58 ± 11.22	−4.77 ± 12.69	0.921
Redness%	−0.32 ± 36.22	−1.15 ± 40.24	0.893

Note. M = mean; SD = standard deviation. ANOVA.

Table 4
The distribution of treatment efficacy of Vancouver Scar Scale (VSS) between the two groups.

Groups	≤0 %	0%–25 %	25%–50 %	50%–75 %	>75 %	Total
triamcinolone external application	52 (59.1 %)	21 (23.9 %)	11 (12.5 %)	4 (4.5 %)	0 (0 %)	88
triamcinolone intralesional injection	16 (23.9 %)	24 (35.8 %)	23 (34.3 %)	4 (6.0 %)	0 (0 %)	67
Total	68	45	34	8	0	155

Note. P = 0.000, Chi-Square Test.

Table 5
The adverse effects between the two groups.

Groups	triamcinolone external application	triamcinolone intralesional injection	P value	Total
Adverse effects, n (percent)	47 (53.4 %)	37 (55.2 %)	0.172[a]	84 (54.2 %)
oozing	22 (25.0 %)	20 (29.9 %)		42 (27.1 %)
bleeding	14 (15.9 %)	14 (20.9 %)		28 (18.1 %)
swelling	11 (12.5 %)	3 (4.5 %)		14 (9.0 %)

Note. a: Chi-Square Test.

Therefore, ablative fractional laser combined with triamcinolone could increase the clinical efficacy in the improvement of hypertrophic scars.

Moreover, in our study, we compared the two different topical triamcinolone delivery methods, and we found that the VSS (especially the pliability and height score) and hardness decline rate in the laser combined with triamcinolone intralesional injection group were much greater than those in the laser combined with postprocedure topical triamcinolone suspension application group. This result might be due to the deeper penetration and stronger concentration in the injection group. Although ablative fractional laser is an established technique to enhance uptake of topical agents in the skin, the channels created by the laser gradually diminish within hours and re-epithelialize at approximately 2 days [19,20]. Therefore, the penetration time in the topical triamcinolone external application group was shorter than that in the intralesional injection group. Despite the stronger concentration in the injection group, there were no differences in the incidence of adverse effects, including oozing, bleeding, and selling, in our study. When it was combined with laser treatment, the frequency of intralesional injection was decreased from once every two weeks to once every month [21], which can also reduce the incidence of triamcinolone adverse effects.

There is a limitation of the present study. After three treatment sessions for the thicker scars, we found that in both groups, most of the patients had less than 50 % clinical efficacy in the VSS score change. Nevertheless, we found that the scars in some patients were more improved after more than 3 sessions of laser treatment (Fig. 1). The 3 treatment sessions might be short for the improvement of thicker scars. It is better to explore the long-term effects of thicker hypertrophic scars and to determine the optimal number of treatment sessions.

4. Conclusion

This study indicated that ablative fractional carbon dioxide laser combined with triamcinolone is an effective and safe treatment for thicker hypertrophic scars and had a lower risk of adverse effects. The topical triamcinolone intralesional injection delivery had a better treatment outcome than the topical triamcinolone suspension application in thicker hypertrophic scars.

5. Materials and methods

1. Patients

Patients were enrolled from January 2018 to December 2020 from the Institute of Burn Research in the Southwest Hospital of Army

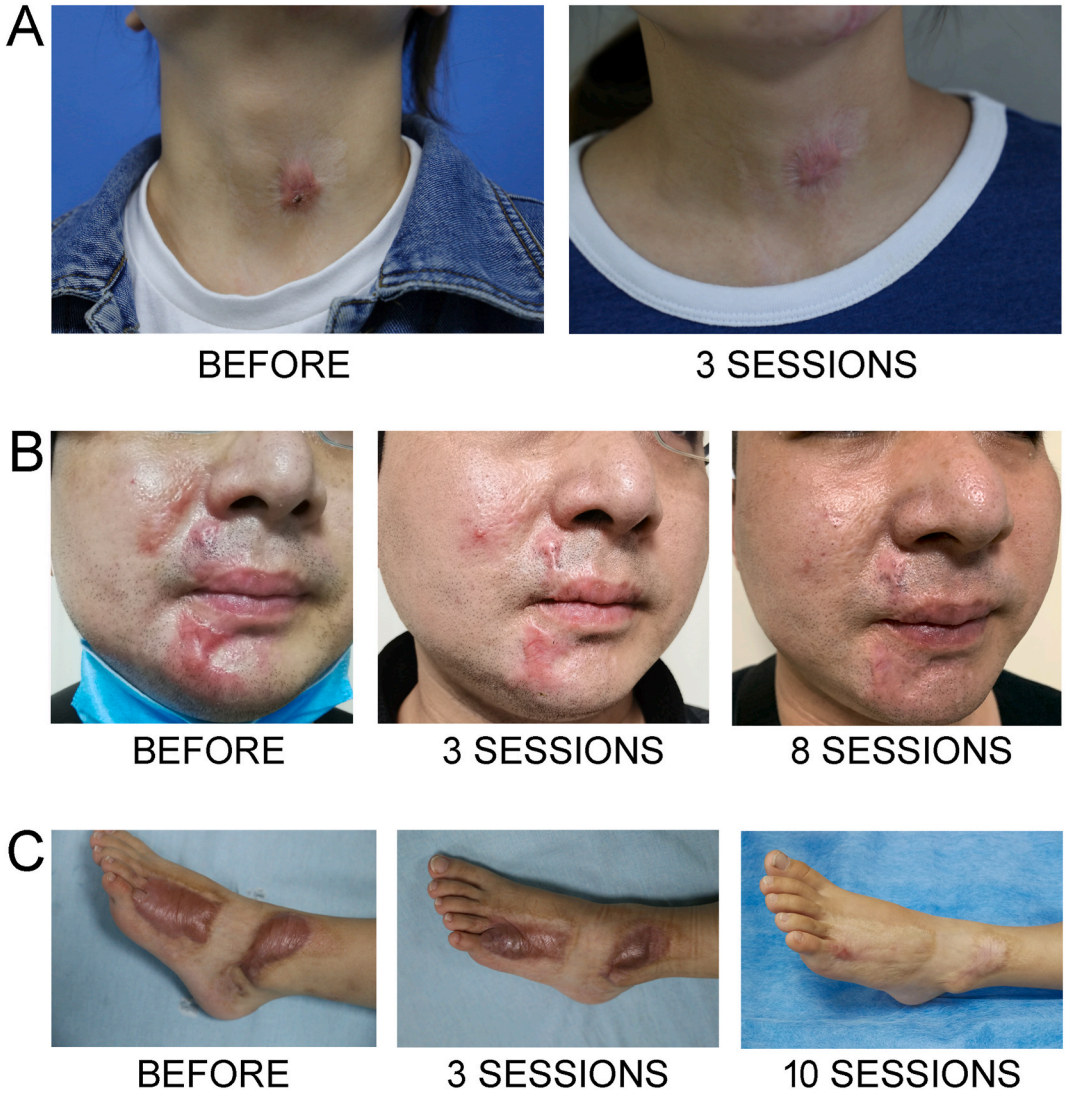

Fig. 1. The photo images of patients before and after ablative fractional CO2 laser treatment assisted with different topical triamcinolone delivery way. A: 19 years old woman suffered with flame injury started to receive laser treatment assisted with triamcinolone external application. The texture and thickness of scar were improved after 3 times of treatment. B: 37 years old man suffered with scald injury started to receive laser treatment assisted with triamcinolone intralesional injection. A significant improvement of scar pigmentation, vascularity, texture and thickness was evident after 8 treatment sessions. C: 14 years old teenager suffered with scald injury started to receive laser treatment assisted with triamcinolone intralesional injection. The scar size, height, texture and color were significant improved after 10 treatment sessions. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Medical University, Chongqing, China. This retrospective study was approved by the Ethics Committee of the First Affiliated Hospital of Army Medical University. All patients signed an informed consent approved by the hospital ethics committee. All the patients' information was kept confidential. The clinical data included demographic information (age and sex), burn injury characteristics, the Vancouver Scar Scale (VSS) score of each patient, the hardness and color of the scar, and the laser treatment parameters.

The inclusion criteria were as follows: 1) height score of VSS $\geq$2; 2) age 14–65 years; 3) the maximal diameter of scar between 0.5 and 5 cm; 4) ablative fractional CO2 laser treatment and triamcinolone were received after injury; and 5) complete information pre- and postlaser treatment.

The exclusion criteria were as follows: 1) active systemic disease, including infection in the treatment area or tumor; and 2) a lack of clinical data.

According to the triamcinolone application, the patients were divided into a triamcinolone external application group and a triamcinolone intralesional injection group.

2. Laser treatment protocol

The ablative fractional carbon dioxide laser (Acupulse, Lumenis Ltd., Israel) was set to deep mode with an energy range of 30 MJ and a density range of 10 %. The superficial mode treatment parameters included an energy range of 150 MJ and a density range of 40 %. The size and shape of the light spot were set according to the size and shape of the scar. All the patients received both the deep mode and superficial mode.

Topical anesthetic lidocaine cream (1 g cream including 25 mg prilocaine and 25 mg lidocaine) (Beijing Ziguang Pharmaceutical CO., Ltd., China) was applied under occlusion for 1 h. Then, the anesthetic cream was cleaned off before the procedure. Alcohol (75 %) was applied around the scar treatment area, and the area was properly dried before laser scanning.

In the triamcinolone external application group, 40 mg/ml triamcinolone acetonide suspension (Kunming Jida Pharmaceutical CO., Ltd., China) was applied directly to ablative laser microcolumns within 2 h after the laser treatment. In the triamcinolone intralesional injection group, triamcinolone was injected intradermally into the scar before the laser therapy and was injected until the scar turned white. The injections were made at different points with a point distance of more than 1 cm. According to the patient's age, physique, and scar size, the injection dosage each time was 10–40 mg. All patients in the two groups received standardized scar care, including daily scar cleaning, scar massage and pressure therapy. All patients received three fractional carbon dioxide laser treatment sessions at 4-week intervals. The patients did not get further application of triamcinolone during the monthly gap between the therapy sessions.

3. Assessment of treatment efficacy

Treatment efficacy and safety in the two groups were evaluated one month after three fractional carbon dioxide laser therapy sessions. Photographs were obtained using a digital camera (Canon, EOS 6D, Canon, Japan) with consistent settings, lighting, and patient positioning at baseline, before each treatment and one month after the final treatment. Two blinded clinicians performed objective clinical evaluations separately using the VSS, which included pigmentation, pliability, height, and vascularity. The two clinicians measured the hardness of the scar independently using a durometer (Shore, HT-6510OO, Guangzhou Landtek Instrument Co., LTD, China). The MiniScan XE Plus spectrocolorimeter (HunterLab, Reston, VA, USA) was employed to evaluate the color of the scar in terms of lightness and redness. The primary outcomes were the total VSS score before laser treatment and at a one-month follow-up after the last laser treatment. The secondary outcomes were the scar hardness measured by durometry and color evaluated by spectrocolorimetry.

According to the effectiveness percentage (effectiveness percentage = [initial value-last value]/initial value*100 %), the treatment effectiveness was categorized into 5 groups: ineffective ($\leq$0 %), mildly effective (0 % -$\leq$ 25 %), moderately effective (25 % -$\leq$ 50 %), significantly effective (50 % -$\leq$ 75 %), and very significantly effective (>75 %).

SPSS 23.0 software (Chicago, IL, U.S.) was used for statistical analysis in this study. The data are expressed as the mean $\pm$ standard deviation (SD). For categorical variables, the data are presented as n (%). The baseline characteristics of the patients and the difference in adverse events between the two groups were determined using chi-squared tests. Comparisons between the pre- and posttreatment values were performed using paired-sample t tests. Comparisons between the two groups were performed using ANOVA. The distribution of treatment efficacy between the two groups was determined using chi-squared tests. $P < 0.05$ was regarded as statistically significant.

Ethics declarations

This retrospective study was approved by the Ethics Committee of the First Affiliated Hospital of Army Medical University (KY2020012).

Data availability statement

All data included in this study are available upon request by contact with the corresponding author.

Additional information

No additional information is available for this paper.

CRediT authorship contribution statement

Junyi Zhou: Writing - original draft, Investigation, Formal analysis, Data curation. **Fen Hao:** Writing - original draft, Investigation, Formal analysis, Data curation. **Ling Huang:** Data curation. **Qingqing Fu:** Investigation. **Lili Yuan:** Methodology. **Gaoxing Luo:** Supervision. **Jianglin Tan:** Writing - review & editing, Writing - original draft, Supervision, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Jianglin Tan reports financial support was provided by National Natural Science Foundation of China (82072188) and State Key

Laboratory of Trauma, Burn and Combined Injury (SKLZZ201802).

References

[1] E. Shirakami, S. Yamakawa, K. Hayashida, Strategies to Prevent Hypertrophic Scar Formation: a Review of Therapeutic Interventions Based on Molecular Evidence, vol. 8, Burns & trauma, 2020, https://doi.org/10.1093/burnst/tkz003 tkz003.

[2] C.C. Finnerty, M.G. Jeschke, L.K. Branski, J.P. Barret, et al., Hypertrophic scarring: the greatest unmet challenge after burn injury, Lancet 388 (10052) (2016) 1427–1436, https://doi.org/10.1016/s0140-6736(16)31406-4.

[3] N.C. Henderson, F. Rieder, T.A. Wynn, Fibrosis: from mechanisms to medicines, Nature 587 (7835) (2020) 555–566, https://doi.org/10.1038/s41586-020-2938-9.

[4] E. Eremenko, J. Ding, P. Kwan, E.E. Tredget, The biology of extracellular matrix proteins in hypertrophic scarring, Adv. Wound Care 11 (5) (2022) 234–254, https://doi.org/10.1089/wound.2020.1257.

[5] N. Bouzari, S.C. Davis, K. Nouri, Laser treatment of keloids and hypertrophic scars, Int. J. Dermatol. 46 (1) (2007) 80–88, https://doi.org/10.1111/j.1365-4632.2007.03104.x.

[6] R.R. Anderson, M.B. Donelan, C. Hivnor, E. Greeson, et al., Laser treatment of traumatic scars with an emphasis on ablative fractional laser resurfacing: consensus report, JAMA dermatology 150 (2) (2014) 187–193, https://doi.org/10.1001/jamadermatol.2013.7761.

[7] J.S. Waibel, A.J. Wulkan, P.R. Shumaker, Treatment of hypertrophic scars using laser and laser assisted corticosteroid delivery, Laser Surg. Med. 45 (3) (2013) 135–140, https://doi.org/10.1002/lsm.22120.

[8] D. Wolfram, A. Tzankov, P. Pülzl, H. Piza-Katzer, Hypertrophic scars and keloids–a review of their pathophysiology, risk factors, and therapeutic management, Dermatol. Surg. 35 (2) (2009) 171–181, https://doi.org/10.1111/j.1524-4725.2008.34406.x.

[9] K.M. Klifto, M. Asif, C.S. Hultman, Laser management of hypertrophic burn scars: a comprehensive review, Burns Trauma 8 (2020), https://doi.org/10.1093/burnst/tkz002 tkz002.

[10] P. Sun, X. Lu, H. Zhang, Z. Hu, The efficacy of drug injection in the treatment of pathological scar: a network meta-analysis, Aesthetic Plast. Surg. 45 (2) (2021) 791–805, https://doi.org/10.1007/s00266-019-01570-8.

[11] M. Bi, P. Sun, D. Li, Z. Dong, et al., Intralesional injection of botulinum toxin type A compared with intralesional injection of corticosteroid for the treatment of hypertrophic scar and keloid: a systematic review and meta-analysis, Med. Sci. Mon. Int. Med. J. Exp. Clin. Res. : international medical journal of experimental and clinical research 25 (2019) 2950–2958, https://doi.org/10.12659/msm.916305.

[12] Z. Zhuang, Y. Li, X. Wei, The safety and efficacy of intralesional triamcinolone acetonide for keloids and hypertrophic scars: a systematic review and meta-analysis, Burns, journal of the International Society for Burn Injuries 47 (5) (2021) 987–998, https://doi.org/10.1016/j.burns.2021.02.013.

[13] A. Trisliana Perdanasari, M. Torresetti, L. Grassetti, F. Nicoli, et al., Intralesional injection treatment of hypertrophic scars and keloids: a systematic review regarding outcomes, Burns & trauma 3 (2015) 14, https://doi.org/10.1186/s41038-015-0015-7.

[14] S.W. Kim, Management of keloid scars: noninvasive and invasive treatments, Archives of plastic surgery 48 (2) (2021) 149–157, https://doi.org/10.5999/aps.2020.01914.

[15] W. Manuskiatti, C. Yan, O. Artzi, M.K.R. Gervasio, et al., 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, Lasers in Surgery and Medicine, 2021, https://doi.org/10.1002/lsm.23511.

[16] E. Wenande, R.R. Anderson, M. Haedersdal, Fundamentals of fractional laser-assisted drug delivery: an in-depth guide to experimental methodology and data interpretation, Adv. Drug Deliv. Rev. 153 (2020) 169–184, https://doi.org/10.1016/j.addr.2019.10.003.

[17] G. Fredman, E. Wenande, K. Hendel, K. Togsverd-Bo, et al., Efficacy and safety of laser-assisted combination chemotherapy: a follow-up study of treatment with 5-fluorouracil and cisplatin for basal cell carcinoma, Laser Surg. Med. 54 (1) (2022) 113–120, https://doi.org/10.1002/lsm.23497.

[18] E. Wenande, U.H. Olesen, S. Stürup, C.M. Lerche, et al., Laser-assisted delivery enhances topical uptake of the anticancer agent cisplatin, Drug Deliv. 25 (1) (2018) 1877–1885, https://doi.org/10.1080/10717544.2018.1534896.

[19] C.A. Banzhaf, D. Thaysen-Petersen, C. Bay, P.A. Philipsen, et al., Fractional laser-assisted drug uptake: impact of time-related topical application to achieve enhanced delivery, Laser Surg. Med. 49 (4) (2017) 348–354, https://doi.org/10.1002/lsm.22610.

[20] C.A. Banzhaf, B.S. Wind, M. Mogensen, A.A. Meesters, et al., Spatiotemporal closure of fractional laser-ablated channels imaged by optical coherence tomography and reflectance confocal microscopy, Laser Surg. Med. 48 (2) (2016) 157–165, https://doi.org/10.1002/lsm.22386.

[21] H. Song, J. Tan, Q. Fu, L. Huang, et al., Comparative efficacy of intralesional triamcinolone acetonide injection during early and static stage of pathological scarring, J. Cosmet. Dermatol. (2018), https://doi.org/10.1111/jocd.12690.