Received: 11 November 2021 | Revised: 1 February 2022 | Accepted: 1 February 2022

DOI: 10.1111/iwj.13775

ORIGINAL ARTICLE

IWJ WILEY

Combination of fractional carbon dioxide laser and topical triamcinolone vs intralesional triamcinolone for keloid treatment: A randomised clinical trial

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Funding information
This work was supported by the Medical Research Council (grant number 60-016-10-1).

Abstract

To compare the therapeutic effect of fractional carbon dioxide (CO_2) laser + topical triamcinolone (TA) with intralesional TA on keloids. Twenty-two participants were randomised into two groups: group A, treated with fractional CO_2 laser + topical TA, and group B, treated with intralesional TA. The interventions were performed at every 4-week interval until the keloids were resolved or at the completion of 1 year. At each session, the scar volume, Vancouver Scar Scale (VSS) were assessed. Recurrence was observed for 1 year. The mean scar volumes and VSS scores were not significantly different between the two groups. After 1 year, the scar volume change in group B was greater than group A (86.5% vs 59.1%, *P*-value = .016). The mean VSS scores were significantly decreased in group A (8.0 ± 1.5 to 4.8 ± 1.6, *P*-value <.001) and group B (8.4 ± 0.8 to 4.8 ± 1.6, *P*-value <.001). The keloids were completely resolved in 63.6% and 72.7% of the patients, and recurrence was observed in 9.1% and 18.2% of the patients in groups A and B, respectively. The combination of fractional CO_2 laser with topical TA was an alternative option for the treatment of keloids.

KEYWORDS

fractional carbon dioxide laser, intralesional triamcinolone, keloid treatment, topical triamcinolone

Key Messages

- there are a wide variety of keloid treatments, such as surgery, intralesional steroid injection, laser, and cryosurgery
- the aim of the study was to compare the therapeutic effect of fractional carbon dioxide laser and topical triamcinolone (TA) with intralesional TA in 22 patients with keloids
- this result showed a significant improvement in the keloids, by a significant reduction in scar volume and the VSS score in both groups
- this is the first study to report the effective outcomes of ablative laser with topical TA in keloid treatment

1 | INTRODUCTION

Keloid scar is the result of an abnormal wound healing process. It can have a negative psychological impact on patients due to its aesthetically displeasing appearance. Furthermore, the presence of an itching sensation, pain, and discomfort might, subsequently, affect the quality of life of the patient. Keloid formation is thought to be caused by an imbalance between the synthesis and degradation of extracellular matrix collagen, resulting in increased fibroblast density and proliferation rates.[1]

Currently, a wide variety of keloid treatments, including surgery, intralesional steroid injection, laser, and cryosurgery, are available.[2] Intralesional steroid injection is the first-line treatment among physicians. Steroids act as fibroblast growth inhibitors by increasing collagen degradation. However, the potential side effect of this method is the severe pain during the injection, which leads to the abandonment of the treatment followed by an unsatisfactory outcome. Moreover, atrophy of the skin and fat tissues, hypopigmentation, and telangiectasia result in cosmetic dissatisfaction.[3,4] Laser treatment is a more popular option, due to patient cooperation, less pain, and better aesthetics. Evidence suggests that carbon dioxide (CO_2) laser monotherapy can ablate keloids; however, it is associated with high rates of recurrence.[5]

The present study aimed to compare the therapeutic effects and recurrent outcomes of two modalities, the combination of fractional CO_2 laser and topical steroid vs intralesional steroid, for the treatment of keloids within a 2-year period.

2 | MATERIALS AND METHODS

2.1 | Study population

This prospective, randomised controlled study was performed at the Plastic and Reconstructive Surgery Outpatient Department and operating room in the Songklanagarind Hospital from January 2018 to December 2019. The study protocol was approved by the Human Research Ethics Committee, Faculty of Medicine, Prince of Songkla University, and registered in the Thai Clinical Trials Registry (TCTR20211104003), and informed consent was obtained from each patient. Adult patients with keloids were enrolled. The exclusion criteria for the study were as follows: pregnant patients; a history of herpes zoster infection; an immunocompromised status; the presence of infections or skin diseases; a history of steroid and lidocaine allergy; and a history of keloid treatment within the past 1 year.

The patients were randomised in block sizes of four and assigned to two groups: group A, which received fractional CO_2 laser with topical triamcinolone (TA), and group B, which received intralesional TA alone. The laser procedure and intralesional steroid injection were performed by a single plastic surgeon (N.T.) who was unblinded to the treatment groups and took photos of the scars during each visit. Another surgeon (P.P.) assessed the photographs and recorded the outcomes of all the patients at each visit.

The laser procedures were performed in an operating room. Topical anaesthetic cream (EMLA; a proprietary acronym for *eutectic mixture of local anaesthetics*) was applied over the keloid for 45 minutes before the procedure. The fractional CO_2 laser (eCO_2, Lutronic Co., Ltd, Seoul, Korea) was set using the following parameters: static mode, beam size, 120 μm (mm); power, 30 watts; pulse energy, 30 millijoules; and density, 200 spots per square-centimetre (cm^2). The fractional CO_2 laser was performed with a single pass. Subsequently, TA (40 mg/cm^3) diluted (1:1) with 1% xylocaine + adrenaline (1:200 000) was applied over the scar immediately after the procedure, then occluded under a transparent film dressing for 30 minutes, and the solution was allowed to dry without being wiped off. Then, 0.1% TA cream was prescribed for use twice a day for 1 week after the laser treatment. For the intralesional TA group, the TA solution (40 mg/cm^3) was diluted (1:1) with 1% xylocaine + adrenaline (1:200 000) and injected into the keloid scar using a 29-gauge insulin needle.

The Vancouver Scar Scale (VSS) score and scar volume were evaluated via photographic recordings during the monthly visits until the completion of 1 year. Moreover, the pain scores were assessed during the procedure and at 1 minute after the procedure during each of the monthly visits. The VSS evaluations included the vascularity, height/thickness, pliability, and pigmentation of the keloid. The total score was 13.[6,7] The scar volume measurement recorded the maximum width, length, and thickness of the scar in mm, and the estimated scar volume was calculated in mm^3.[8] The pain score was determined via self-assessment using the visual analogue scale (VAS), a 10-cm scale that ranges from no pain to extremely unbearable pain.[9] All patients were followed up at every 2-month interval for 1 year. The VSS, scar volume, presence of complications, and recurrence rates were assessed during every visit (Figure 1).

2.2 | Statistical analysis

All baseline data are presented as mean (*SD*) for continuous variables, numbers (%) for categorical variables, and median (interquartile range; IQR) for original variables. Normality was checked using the Shapiro-Wilk test. The paired *t*-test or Wilcoxon signed-rank test was used to analyse the differences between continuous and ordinal variables, respectively, within the same group. The

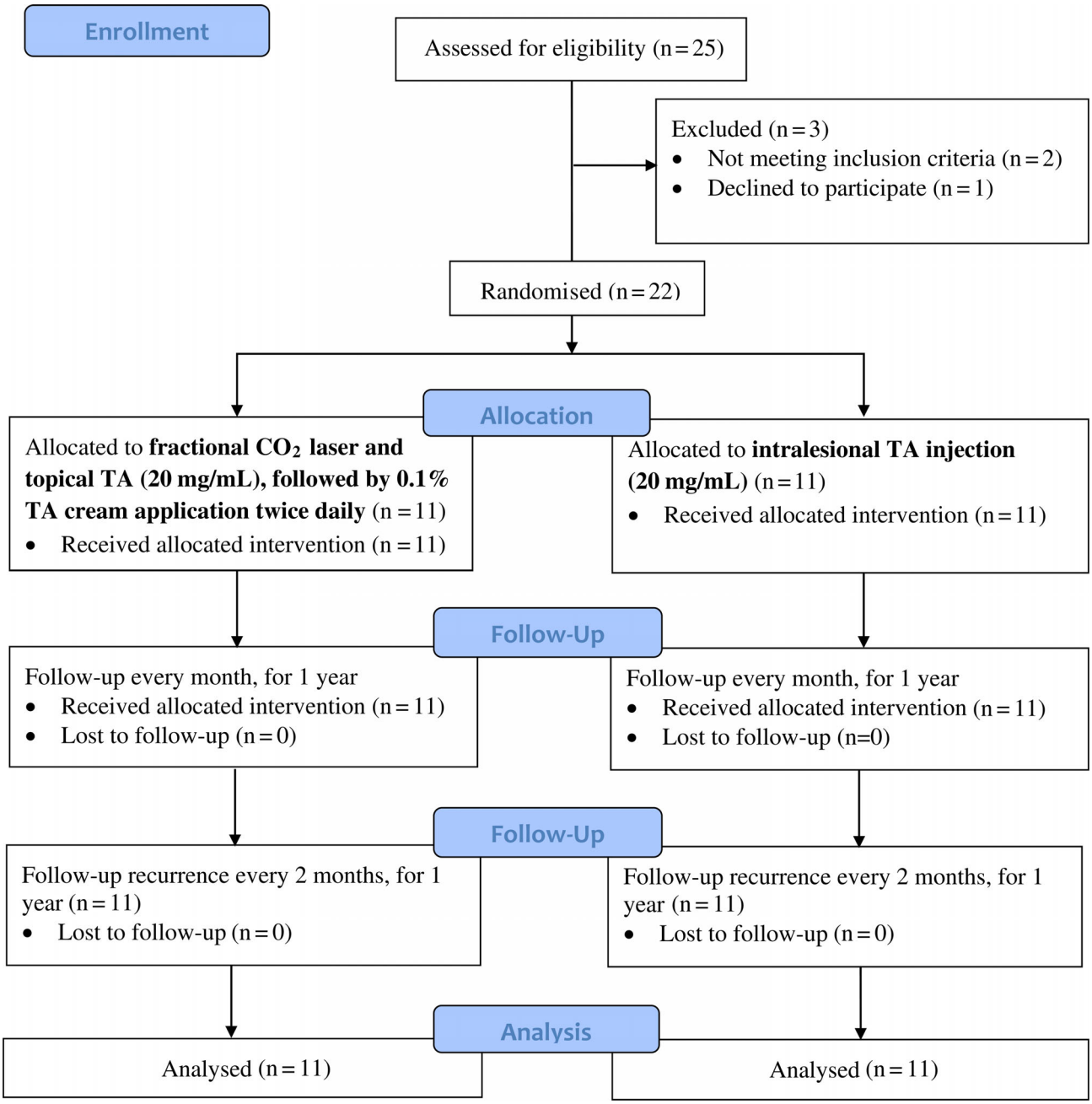

FIGURE 1 Flowchart of clinical study design based on CONSORT statement

generalised linear mixed model was used to compare data between groups before and during every session during the treatment and follow-up periods. All statistical analyses were performed using the Epidata software (version 3.1) and R (version 3.5.1). A *P*-value of <.05 was considered to be statistically significant.

3 | RESULTS

The mean age of the 22 patients enrolled in this study was 44.8 ± 19.9 years in group A (n = 11) and 42.6 ± 18.3 years in group B (n = 11). Females were predominant in both the groups. The major causes of keloid were trauma (45.5%) and surgery (36.4%) in group A and acne (36.4%) and surgery (36.4%) in group B. In group A, the keloids were most commonly present on the chest (63.6%), followed by the extremities (18.2%), abdomen (9.1%), and ear (9.1%). In group B, the keloids were predominantly observed on the chest (36.4%), followed by the extremities (18.2%) and abdomen (18.2%). The baseline estimated scar volume and VSS scores were not significantly different between the two groups (Table 1).

The average number of treatment visits was 10.5 ± 2.6 in group A and 6.3 ± 3.0 in group B. In group A, the mean scar volume significantly decreased from 5608.4 ± 7251.0 mm^3 before treatment to 2744.3 ± 5619.3 mm^3 after treatment (*P*-value <.001). Likewise, the mean scar volume significantly decreased from 3944.8 ± 4368.6 mm^3 before treatment to 286.6 ± 412.9 mm^3 after treatment in group B (*P*-value <.001). Significant decreases in scar volume were observed after 2 months in group B and after 4 months in group A. The percentage of scar volume change in group B was greater than that in group A at the end of the 1-year treatment (86.5% vs 59.1%; *P*-value = .016; Figure 2). After the treatment, the mean VSS scores significantly decreased from 8.0 ± 1.5 to 4.8 ± 1.6 (*P*-value <.001) and from 8.4 ± 0.8 to 4.8 ± 1.6 (*P*-value <.001) in groups A and B, respectively. However, no statistically significant difference was observed between the groups at the 1-year treatment interval (*P*-value = 1.000; Figure 3).

At the end of the 1-year follow-up period, the estimated scar volumes were found to be significantly decreased in both groups (2605.4 ± 5681.0 mm^3 and 210.4 ± 412.2 mm^3 in groups A and B, respectively). Moreover, the change in scar volume (%) in group B was greater than that in group A (90.1% vs 64.8%; *P*-value = .031). However, no significant difference in the mean VSS score was observed between the two groups.

The keloids were resolved after the 1-year treatment period in 7 out of 11 patients (63.6%) in group A and 8 out of 11 patients (72.7%) in group B. Recurrent keloids were observed in only 1 patient (9.1%) in group A and in 2 patients (18.2%) in group B. Furthermore, 3 patients (27.3%) in group A and 1 patient (9.1%) in group B

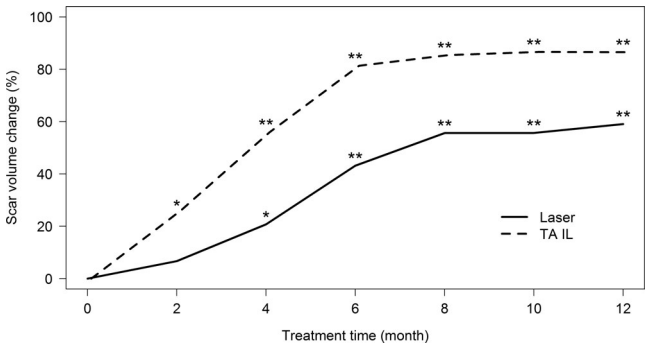

FIGURE 2 Changes in scar volume during the 1-year treatment period. **P*-value (pre- post-treatment) <.05, ***P*-value (pre- post-treatment) <.001

TABLE 1 Demographic characteristics of the participants (n = 22)

Characteristics	Group A (n = 11)	Group B (n = 11)	*P*-value
Age (y), mean (*SD*)	44.8 (19.9)	42.6 (18.3)	.792
Gender, n (%)			.659
Male	5 (45.5)	3 (27.3)	
Female	6 (54.5)	8 (72.7)	
Cause, n (%)			.132
Acne	0 (0)	4 (36.4)	
Infection	0 (0)	1 (9.1)	
Piercing	1 (9.1)	0 (0)	
Surgery	4 (36.4)	4 (36.4)	
Trauma	5 (45.5)	1 (9.1)	
Vaccination	1 (9.1)	1 (9.1)	
Site of scar, n (%)			.859
Chest	7 (63.6)	4 (36.4)	
Extremities	2 (18.2)	2 (18.2)	
Abdomen	1 (9.1)	2 (18.2)	
Ear	1 (9.1)	1 (9.1)	
Breast	0 (0)	1 (9.1)	
Flank	0 (0)	1 (9.1)	
Estimated scar volume (mm^3), mean (*SD*)	5608.4 (7251.0)	3944.8 (4368.6)	.522
VSS score, mean (*SD*)	8.0 (1.5)	8.4 (0.8)	.498

Abbreviations: mm^3, cubic millimetres; n, number; *SD*, standard deviation; VSS, Vancouver Scar Scale.

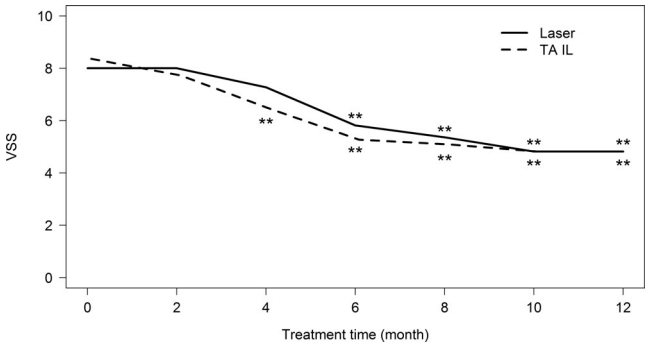

FIGURE 3 Vancouver Scar Scale scores during the 1-year treatment period. VSS, Vancouver Scar Scale. ***P*-value (pre- post-treatment) <.001

presented with partial resolution and a volume reduction of less than 50.0% after the treatment.

The mean VAS scores tended to be higher in group B of 2.2 (1.3, 4.1) compared with group A of 1.3 (1.1, 2.1) (*P*-value = .178). The pain scores were significantly decreased 1 minute after the procedure in both groups (*P*-value <.001 and *P*-value = .004, respectively); however, no significant difference was observed between the two groups. Six out of 11 patients in group B presented with adverse events: 4 patients experienced hypopigmentation and 2 presented with lipodystrophy. No adverse events were observed in patients from group A.

4 | DISCUSSION

This study showed a significant improvement in the keloids, as demonstrated by the significant reduction in scar volume and the VSS score in both groups. Intralesional TA tended to improve the condition more rapidly within the first 6 months when compared with the laser group. However, the treatment response after 1 year was not significantly different in the two groups. During the follow-up period, the rate of complete resolution of the keloid was similar (approximately 60.0%-70.0%) in both groups, and recurrence was observed in very few patients.

In previous studies, laser treatment for keloids mainly focused on the use of a pulse dye laser (PDL), a non-ablative laser therapy that improves erythema and the pliability of the hypertrophic scar.[10] However, PDL monotherapy is not sufficient to completely resolve the keloid. Recent evidence indicates that ablative laser therapy can reduce both hypertrophic and keloid scars.[5] Fractional CO_2 generates multiple small holes in the scar and leads to collagen remodelling and faster scar repair while maintaining the integrity of the epidermis.[11] Ablative laser-assisted drug delivery will increase drug penetration beyond the stratum corneum and enhance the effect of topical steroids while minimising tissue damage. The study by Mamalis et al showed that CO_2 ablation monotherapy is effective for keloids, but the recurrence rate was high (74.0%-89.0%) within a 2-year period.[5] CO_2 laser therapy combined with adjuvant therapies, such as intralesional steroid injection or occlusive agents, showed promising outcomes in reducing the recurrence of keloids.[2] However, steroid injections may cause side effects such as telangiectasias, hypopigmentation, and atrophy.[12]

In the current study, topical steroids were directly applied to the keloid scar immediately after fractional CO_2 treatment in group A. Improvements in the keloids, in terms of VSS and scar volume, were observed in both groups after the 1-year treatment. This finding is similar to that reported by Abd El-Dayem et al, wherein VSS improvement was observed following both procedures, ablative erbium laser with occluded topical steroid cream dressing and intralesional steroid injection, at the 12-week follow-up period.[13] However, keloid resolution was observed in nearly 64.0% of the patients in group A (CO_2 laser with topical steroids) in the present study, which was slightly higher than that reported in the study by Cavalié et al (50.0%) after treatment with erbium laser + topical betamethasone.[14] The recurrent rate of 9.1% in group A during the 1-year follow-up period in the current study was much smaller than that reported by Cavalié et al (recurrent rate, 22.0% within 8 months of follow-up).[14]

A few patients did not respond well to laser treatment with topical TA in the present study, which might be attributed to the keloids having a high raised scar. Previous studies have reported that keloids with increased scar heights will not respond well to laser treatment due to the inability of the beam to reach the targeted depth. The depth of ablation of the laser is an important factor because it is directly correlated with the treatment efficacy. The penetration of the laser typically extends up to 50-2000 μm inside the dermis; hence, the deeper dermal fibrotic components might be left untreated.[15,16] Thus, keloids with increased heights should be treated by methods other than laser treatment.

Due to the limitation of maximum daily dose of TA injection (1 mg/kg/d) in one treatment session, the use of laser treatment with topical TA might be better in cases of the keloids with widened scar area, in which bigger amounts of drugs are required. Pain during the procedure was significantly lower in group A compared with that in group B in the present study. Park et al reported a mean pain score of 1.1 in 10.0 in the laser treatment group.[17] Application of the topical anaesthetic

cream before the procedure and the use of xylocaine during the intralesional injection might account for the patient cooperation in the current study. However, the absence of any significant difference in pain after treatment between the two groups might be due to the effect of the anaesthetic.

This was a randomised controlled study with a control group; keloid scars from several sites and a variety of causes were included in the study. However, owing to differences in the techniques used for the interventions, there were some difficulties in blinding the patients and the intervention operators. This is the first study to report the use of the TA solution along with ablative laser treatment. Most studies used a topical steroid cream with an occlusive dressing. Furthermore, most previous studies used ablative laser therapy with erbium yttrium aluminium garnet, whereas CO_2 laser with fractional mode was used in the current study. The CO_2 laser with fractional mode was a basic laser type, which was practical in most hospitals. Lastly, our study followed the patients for 1 year after treatment completion. Thus, we can observe the keloid recurrence. The limitation of the present study was the relatively small sample size, which might potentially mask the significance of the results.

Future studies are necessary to explore the effectiveness of other topical agents such as 5-fluorouracil, bleomycin, high-potency steroids, silicone gels, or occlusive dressings in conjunction with ablative laser therapy for the treatment of keloids. Moreover, it might be interesting to determine the optimal laser setting for superior therapeutic outcomes and the optimal number of laser treatment sessions required in the future. In conclusion, the combination of fractional CO_2 laser with topical TA was an alternative option for the treatment of keloids without any adverse effects.

ACKNOWLEDGEMENTS

The authors thank Miss Nannapat Pruphetkaew for her assistance with data analysis.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

All authors contributed to the conception and design of the study. Material preparation, data collection, and analysis were performed by Pitchaya Pliensiri and Niti Tawaranurak. The first draft of the manuscript was written by Krongthong Tawaranurak, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

ETHICS STATEMENT

The Ethics Committee of the Faculty of Medicine in Prince of Songkla University approved our study (REC 60-016-10-1).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

REFERENCES

1. Berman B, Maderal A, Raphael B. Keloids and hypertrophic scars: pathophysiology, classification, and treatment. *Dermatol Surg*. 2017;43(Suppl 1):S3-S18.
2. Betarbet U, Blalock TW. Keloids: a review of etiology, prevention, and treatment. *J Clin Aesthet Dermatol*. 2020;13:33-43.
3. Wu WS, Wang FS, Yang KD, Huang CC, Kuo YR. Dexamethasone induction of keloid regression through effective suppression of VEGF expression and keloid fibroblast proliferation. *J Invest Dermatol*. 2006;126:1264-1271.
4. Boyadjiev C, Popchristova E, Mazgalova J. Histomorphologic changes in keloids treated with Kenacort. *J Trauma*. 1995;38:299-302.
5. Mamalis AD, Lev-Tov H, Nguyen DH, Jagdeo JR. Laser and light-based treatment of keloids – a review. *J Eur Acad Dermatol Venereol*. 2014;28:689-699.
6. Sullivan T, Smith J, Kermode J, McIver E, Courtemanche DJ. Rating the burn scar. *J Burn Care Rehabil*. 1990;11:256-260.
7. Nedelec B, Shankowsky A, Tredgett EE. Rating the resolving hypertrophic scar: comparison of the Vancouver Scar Scale and scar volume. *J Burn Care Rehabil*. 2000;21:205-212.
8. Fearmonti R, Bond J, Erdmann D, Levinson H. A review of scar scales and scar measuring devices. *Eplasty*. 2010;10:e43.
9. McCormack HM, Horne DJ, Sheather S. Clinical applications of visual analogue scales: a critical review. *Psychol Med*. 1988;18:1007-1019.
10. Cannarozzo G, Sannino M, Tamburi F, Morini C, Nisticò SP. Flash-lamp pulsed-dye laser treatment of keloids: results of an observational study. *Photomed Laser Surg*. 2015;33:274-277.
11. 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;31:9-18.
12. Ledon JA, Savas J, Franca K, Chacon A, Nouri K. Intralesional treatment for keloids and hypertrophic scars: a review. *Dermatol Surg*. 2013;39:1745-1757.
13. Abd El-Dayem DH, Nada HA, Hanafy NS, Elsaie ML. Laser-assisted topical steroid application versus steroid injection for treating keloids: a split side study. *J Cosmet Dermatol*. 2021;20:138-142.
14. Cavalié M, Sillard L, Montaudié 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;28:74-78.

15. Hunzeker CM, Weiss ET, Geronemus RG. Fractionated CO_2 laser resurfacing: our experience with more than 2000 treatments. *Aesthet Surg J*. 2009;29:317-322.
16. Sardana K, Garg VK, Arora P, Khurana N. Histological validity and clinical evidence for use of fractional lasers for acne scars. *J Cutan Aesthet Surg*. 2012;5:75-90.
17. Park JH, Chun JY, Lee JH. Laser-assisted topical corticosteroid delivery for the treatment of keloids. *Lasers Med Sci*. 2017;32:601-608.

How to cite this article: Tawaranurak N, Pliensiri P, Tawaranurak K. Combination of fractional carbon dioxide laser and topical triamcinolone vs intralesional triamcinolone for keloid treatment: A randomised clinical trial. *Int Wound J*. 2022;19(7):1729-1735. doi:10.1111/iwj.13775