Received: 13 March 2020 | Revised: 26 May 2020 | Accepted: 16 June 2020

DOI: 10.1111/jocd.13564

ORIGINAL CONTRIBUTION

JCD Journal of Cosmetic Dermatology

WILEY

Ablative fractional CO_2 laser vs lyophilized growth factor intralesional injection vs combination of both modalities for striae distensae treatment

Mahmoud Abdallah MD[1] | Hossam Fahmy MD[2] | Shawkat Abdel Hameed MB, BCH[1] | Azza E. Mostafa MD[1]

[1]Department of Dermatology, Venereology and Andrology, Ain Shams University, Cairo, Egypt

[2]Clinical Pathology Department, Ain Shams University, Cairo, Egypt

Correspondence
Azza E. Mostafa, Department of Dermatology, Venereology and Andrology, Faculty of Medicine, Ain Shams University, PO: 11381, Cairo, Egypt.
Email: azzadermpath@gmail.com

Abstract

Background: Different studies had evaluated the efficacy of fractional CO_2 laser and platelet-rich plasma (PRP) in treating striae distensae (SD). Lyophilized growth factors (LGF) represent another form of delivering growth factors similar to PRP with a more standardized method. To the best of our knowledge, no previous trials have been reported using LGF in SD.

Aims: We aimed to compare the efficacy of ablative fractional CO_2 laser vs intralesional injection of LGF vs combination of both modalities for SD treatment.

Methods: This study included 20 female patients with SD. All patients received three modalities of treatment in separate three areas: area A: received fractional CO_2 laser, area B: received combination of fractional CO_2 laser and intradermal injection of LGF, and area C: received intradermal injection of LGF. Each area received three sessions with 6-week intervals. The outcome was evaluated clinically and histopathologically before treatment and six weeks after the last session.

Results: There was a statistically significant clinical and histopathological improvement of SD both in areas A and B after treatment. Area C exhibited nonsignificant clinical and histopathological improvement. Area B showed the best improvement results as compared to areas A and C.

Conclusion: We reported that fractional CO_2 laser combined with LGF injection was more effective than fractional CO_2 laser alone in SD treatment based on clinical and histopathological assessment. We do not advocate LGF as a monotherapy for SD treatment; instead, LGF can be used as a combined therapy with fractional CO_2 laser to improve its outcome.

KEYWORDS

Fractional carbon dioxide laser, lyophilized growth factors, striae distensae

1 | INTRODUCTION

Striae distensae (SD) are prevalent atrophic dermal scars caused by skin overstretching with a considerable psychosocial impact. Several treatment modalities have been tried with varying grades of improvement in SD.[1]

Ablative fractional CO_2 laser (10 600 nm) and platelet-rich plasma (PRP) are among the various modalities used for SD.[1-5] Both

modalities have been used as a monotherapy or combined therapy with other modalities for SD with varying degrees of success.[6,7] The fractional ablative 10 600 nm CO_2 laser is known to generate cutaneous small columns of thermal damage termed microthermal zones where epidermal and dermal coagulation occurs. This thermal injury provokes epidermal and dermal regeneration which eventually improves SD.[8]

When used for SD, PRP resulted in epidermal and dermal regeneration through the release of platelet-derived factors contained in platelet alpha granules namely platelet-derived growth factor α and β, transforming growth factor β1 and β 2, epidermal growth factor, fibroblast growth factor, and vascular endothelial growth factor. These factors stimulate epithelial cells and fibroblasts resulting in epidermal healing with new collagen and elastin formation.[1] Different methods are used to obtain PRP, and consequently, PRP shows variation in the number of platelets and concentration of growth factors. The lack of standardization for the ideal number of platelets in the PRP has a definite influence on the clinical results.[9]

Lyophilized growth factors (LGF) represent a refined form of platelet growth factors based on the use of allogeneic platelets with a predefined standardized number as a source of growth factors instead of autologous platelets used in PRP.[10] To the best of our knowledge, no previous studies had evaluated the therapeutic effect of LGF in SD. We aimed to evaluate the efficacy of allogeneic LGF intralesional injection vs fractional CO_2 laser vs combination of both modalities for SD treatment.

2 | METHODOLOGY

A total of 20 female patients were enrolled in this prospective nonrandomized comparative study. They were recruited during the period from May 2017 to March 2018 after signing an informed consent for the purpose, steps, possible risks, and for the clinical photography. The study was conducted according to the Declaration of Helsinki Principles and was approved by the local ethical committee.

Inclusion criteria were female subjects aged ≥18 years with SD who were clinically free of other dermatologic or systemic diseases. Exclusion criteria included patients who had undergone any surgical treatment procedure for SD prior to the study, for example, laser, radiofrequency, dermabrasion, chemical peeling, and patients who had received systemic retinoids (within six months of study initiation) and/or immunosuppressive drugs. We also excluded patients with history of keloids or hypertrophic scars, connective tissue disease, liver disease, kidney disease, heart disease, diabetes, skin infections, photodermatoses, malignant diseases, skin cancer, and pregnant or lactating females. All patients were subjected to complete history taking including onset, course and duration of the disease, predisposing factors, previous treatments, thorough general examination to exclude any systemic diseases, and full dermatologic examination. Investigations such as complete blood count, bleeding and clotting time, liver and kidney function tests were carried out to exclude systemic abnormalities. Dermatologic examination was done to detect the type of striae (rubra, alba), site, and measurement of the width of the largest striae in the treatment area. In each patient, the treatment area was divided into three areas: area A, received fractional CO_2 laser; area B, received combination of fractional CO_2 laser followed by intradermal injection of LGF; and area C, received intradermal injection of LGF.

2.1 | Treatment protocol

Fractional CO_2 laser was performed using FIRE-XEL (BISON Medical CO., LTD). Each patient had 3 sessions with 6 weeks intervals. The selected striae were treated along their entire length, avoiding overlapping pulses. The parameters used were as follows: power 18 watt, spacing 600 μm, dwell time 600 μs, and 1 stacking, with single pass on the striae. During the sessions, protective eye goggles were used for patients and the treating physician and wet gauze pads were used for patients. Topical pridocaine 5% cream was applied for 60 minutes under occlusion before laser sessions. Ice packs for cooling were immediately applied after laser sessions, and the patients were advised to apply a topical fusidic acid 2% cream and zinc oxide cream twice daily for 1 week after the session.

Lyophilized growth factors used in this study were produced according to the European patency number issued in November 2016 by a patented method[11] and were prepared in Cairo Medical Centre Blood Bank (L-GF™) from platelet concentrates obtained from different donors. The platelet concentrates used for L-GF™ production were treated with two methods to ensure its microbiologic safety. First, the platelet concentrates were treated by the Mirasol® Pathogen Reduction Technology System (Terumo BCT, Ltd) utilizing ultraviolet rays and riboflavin that destructed the nucleic acids of any microorganisms and inactivated residual leukocytes in platelet concentrates. The second method was performed by adding a solvent (tri-n-butylphosphate 0.3%—TNBP[C]) and a detergent (1% Tween 20[d]) for 1 hour at 31°C for eliminating enveloped viruses (HIV, HBV, and HCV). In vitro stimulation of platelets was performed by incubation with human Thrombin (500 units/ mm^3, Sigma Chemical Co) at 37°C for 3 hours with the formation of fibrin clot that was removed leaving platelet fluid releasate. The platelet releasates were divided and dispensed in glass vials. The amount of growth factors present in each vial was adjusted to be equal to those derived from 2 million platelets/μL. The lyophilization process was carried out using a freeze-dryer apparatus (Tofflon, 2014-033 CA). Vials of L-GF™ contained a pale yellow round cake of LGF and were stored between 2° and 8°C. Reconstituted L-GF™ vials remained viable for 1 hour when stored between 15° and 22°C.

Upon use, we allowed a vial of L-GF™ to reach ambient temperature. The flip-off seal and rubber bung were removed, and 2 mL of sterile physiological saline was injected by sterile syringe into the L-GF™ vial. The vial was gently swirled for 3 minutes and was allowed to stand at ambient temperature for 5 minutes to ensure complete protein re-hydration. Sterilization of the selected striae was performed by isopropyl alcohol 70%; then, intradermal injection

of the striae was performed throughout their entire strength with a 1 cm distance between injection sites; and 0.1 cc of L-GF™ was injected per point with a 31-gauge insulin syringe. Each patient received 3 sessions with 6-week intervals.

2.2 | Outcome evaluation

Clinical photography for the patients was taken with a Sony (DSC-W530) digital camera (14 megapixel resolution) using identical camera settings, lighting situation, and patient positioning before treatment and six weeks after the last session. Outcome was assessed based on clinical scores and histopathologic examination before treatment and six weeks after the last session. The clinical scores included the following: (a) measuring the width of the largest SD in the treated area, and the score was given according to the percentage of width reduction after treatment; (b) the mean score of two independent blinded dermatologists' assessment of SD appearance, size and color by comparing patient photographs before treatment and after completion of the treatment by six weeks; and (c) the total score of improvement of SD appearance, size and color. Scores (a), (b), and (c) were graded into a quartile scale[6] of 0 (no change, 0%), 1 (mild improvement, 0%-25%), 2 (moderate improvement, 25%-50%), 3 (marked improvement, 50%-75%), and 4 (excellent improvement, 75%-100%). The patients were asked to rate their satisfaction six weeks after the last session, and a patient's satisfaction score graded into a quartile scale[5] was given of 0 (no change), 1 (not satisfied, <25%), 2 (slightly satisfied, 25% to <50%), 3 (satisfied, 50% to <75%), or 4 (very satisfied, ≥75%). Patients were requested to report any procedural complications, including pain, post-inflammatory hyperpigmentation (PIH), persistent erythema (more than one month), infection, or any allergic reactions on a scale of 0 (not detected) or 1 (detected).

For histological evaluation, 4-mm skin punch biopsies were taken from a representative stria from each treatment area before treatment and after 6 weeks from the last treatment session. Biopsy specimens were fixed in 10% buffered formalin, routinely processed, and embedded in paraffin. From the paraffin blocks, 4 μm thick serial sections were cut and prepared for routine hematoxylin and eosin (H&E) stain, Masson's trichrome stain, and Orcein stain for assessment of collagen and elastic fibers, respectively, by a light microscopy (Olympus© CX41). Additionally, sections were examined using Honestech TVR MFC program (VIDBOX® Inc) for measurement of collagen and elastic fiber thickness in Masson's trichrome- and Orcein-stained sections.

2.3 | Statistical analysis

Statistical analyses were performed using Statistical Package for Social Science (SPSS 20.0 for windows; Inc). Descriptive statistics were expressed as mean ± standard deviation (SD) and range for quantitative data and number (n) and percentage (%) for qualitative data. Statistical analysis was carried out using paired sample *t* test of significance when comparing between related samples. A one-way analysis of variance (ANOVA) test was used when comparing between more than two groups of parametric data. Probability (*P* value) was considered significant if ≤.05 and insignificant if >.05.

3 | RESULTS

This study included 20 female patients with SD who have complied with the study plan with no dropouts. Their age ranged from 20 to 37 years (mean = 26.88 years ± 5.14 SD). The demographic and clinical data of the patients are summarized in Table 1.

Concerning SD width reduction after treatment, the mean width of SD in area A decreased significantly ($P < .001$) from 5.06 mm (± 3.77 SD) to 4.07 mm (±4.08 SD). Similarly, the mean SD width in area B decreased significantly ($P < .001$) from 5.38 mm (±3.48 SD) to 3.71 mm (±3.95 SD). Area C exhibited insignificant SD width reduction ($P = .089$) from 5.65 mm (±3.65 SD) to 4.57 mm (±3.54 SD). By comparing the three areas, we detected a statistically significant ($P < .001$) difference in the mean percentage of width reduction

TABLE 1 Demographic and clinical characteristics of the studied patients

Variable	Values
Age (y)	
Range	20-37
Mean ± SD	26.88 ± 5.14
	n (%)-[n = 20]
Fitzpatrick's skin type	
III	10 (50%)
IV	10 (50%)
Type of striae	
Alba	15 (75%)
Rubra	5 (25%)
Duration of striae (months)	
Range	1-17
Mean ± SD	5.58 ± 4.53
Affected sites	
Thighs	7 (35%)
Calves	6 (30%)
Abdomen	5 (25%)
Buttocks	1 (5%)
Shoulders	1 (5%)
Etiology of striae	
Pregnancy	4 (20%)
Corticosteroids use	11 (55%)
Weight loss	5 (25%)

Abbreviations: %, percentage; n, number.

TABLE 2 Comparison between studied areas regarding the clinical scores

Clinical score	Area A (n = 20) Mean ± SD	Area B (n = 20) Mean ± SD	Area C (n = 20) Mean ± SD	ANOVA *F*-ratio	*P*-value
Score of SD width reduction					
Percentage of reduction (%)	27.81 ± 20.80	41.88 ± 24.33	19.46 ± 12.19	11.741	**<.001**
	n (%)	**n (%)**	**n (%)**		
Blinded dermatologists' score					
No change	2 (10)	1 (5)	7 (35)	9.413	**<.001**
Mild improvement	6 (30)	7 (35)	11 (55)		
Moderate improvement	11 (55)	0 (0)	0 (0)		
Marked improvement	1 (5)	11 (55)	2 (10)		
Excellent improvement	0 (0)	1 (5)	0 (0)		
Mean ± SD	1.61 ± 0.84	2.53 ± 1.12	1.07 ± 0.67		
Total improvement score					
No change	0 (0)	0 (0)	6 (30)	27.217	**<.001**
Mild improvement	4 (20.0)	1 (5)	5 (25)		
Moderate improvement	10 (50.0)	6 (30)	5 (25)		
Marked improvement	6 (30.0)	9 (45)	4 (20)		
Excellent improvement	0 (0)	4 (20)	0 (0)		
Mean ± SD	1.84 ± 0.84	2.97 ± 1.95	1.02		
Patient's satisfaction score					
No change	1 (5)	1 (5)	10 (50)	5.224	**.013**
Not satisfied	8 (40)	2 (10)	6 (30)		
Slightly satisfied	9 (45)	5 (25)	3 (15)		
Satisfied	2 (10)	10 (50)	1 (5)		
Very satisfied	0 (0)	2 (10)	0 (0)		
Mean ± SD	1.73 ± 0.83	2.59 ± 1.13	1.14 ± 098		

Note: significant *P* values are in bold.

Abbreviations: %, percentage; n, number.

between the areas where area B showed the highest percentage of reduction (Table 2, Figures 1-3).

The detailed results about the changes in other clinical scores in the studied areas are presented in Table 2, and selected cases are revealed in figures from 1 to 3. Area B exhibited the highest improvement in all clinical scores.

Regarding the reported post-procedural complications, PIH developed in 8 patients (40%) in area A, and the same patients (n = 8, 40%) developed PIH in area B. No PIH was detected in area C. All patients who developed PIH (100%) were of skin type IV. From the 8 patients who developed PIH in areas A and B, 5 patients (62.5%) had stria rubra and 3 patients (37.5%) had stria alba. Comparing between studied areas regarding PIH showed a statistically significant difference ($P = .049$).

Mild tolerable pain was reported in area A in six (30%) patients, in 8 patients (40%) in area B, and in 7 patients (35%) in area C with statistically insignificant ($P = .81$) difference between areas. Pain was temporary and was limited to the time of treatment session. No other side effects were identified.

Histopathological assessment of untreated SD in all areas revealed similar findings. There was thinned epidermis with effaced rete ridges. Collagen fibers were sparse and fragmented (Figure 4A). Elastic fibers were few, unevenly distributed, thin, and fragmented (Figure 5A). Examination of histological slides from the same site after treatment revealed parallel histological changes to various degrees among studied areas. After treatment, there was an increase in the epidermal thickness with improvement of rete ridges pattern. Collagen fibers were regularly aligned, continuous, and thicker (Figure 4B). Elastic fibers increased in number and were regular, longer, and thicker (Figure 5B).

Table 3 presents the changes in collagen fiber and elastic fiber thickness before and after treatment in studied areas that was statistically significant for both collagen fibers and elastic fibers in areas A and B. By comparing the three areas after treatment, we found statistically significant results in the mean difference of increase in collagen fiber thickness ($P < .001$) and in elastic fiber thickness ($P = .042$). Area B showed the highest improvement in the mean difference of increase in collagen and elastic fiber thickness (Table 4).

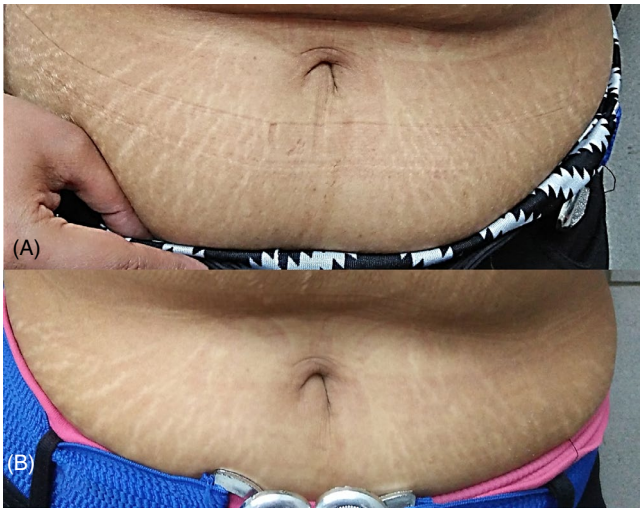

FIGURE 1 A, Clinical photography of a 32-y-old patient with striae alba on her abdomen to history of pregnancy before treatment, and B, clinical photography of the same site showing moderate improvement 6 wk after fractional CO_2 laser treatment

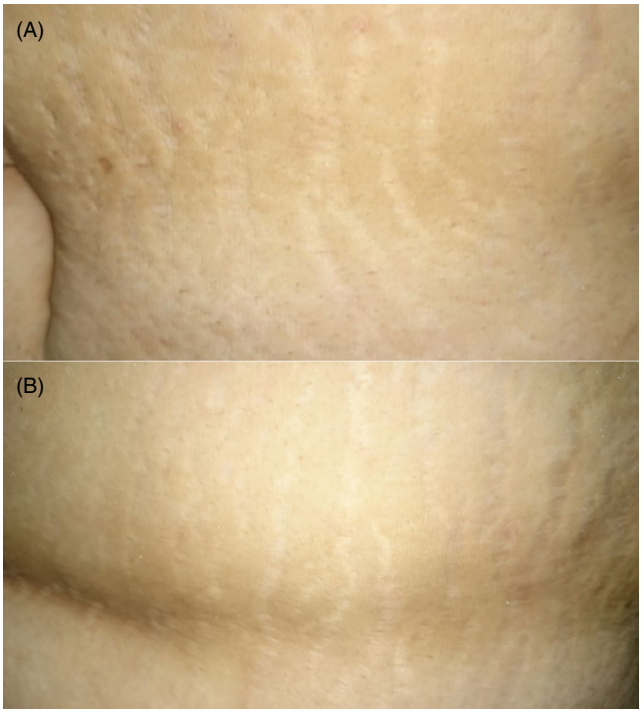

FIGURE 3 A, Clinical photography of a 37-y-old patient with striae alba on her abdomen due to history of pregnancy before treatment, and B, clinical photography of the same site showing mild improvement 6 wk after LGF injection

4 | DISCUSSION

In this study, we evaluated the effect of fractional CO_2 laser vs LGF intralesional injection vs combination of both modalities for SD treatment. The age of patients in our series ranged from 20 to 37 years with a mean of 26.88 years. This age range was in keeping with Kim et al[6] results who suggested that SD occurs around the age of twenties due to puberty, pregnancy, and weight gain that mostly occur around that age in females.

Regarding the width of striae, we reported a statistically significant reduction in SD width in areas treated with fractional CO_2 laser either alone or combined with LGF. Areas that received LGF only exhibited insignificant width reduction after treatment. Likewise, we reported better clinical improvement of SD based on other clinical scores in areas treated with fractional CO_2 laser either alone or combined with LGF. The clinical improvement in SD in our cases was also reflected on the histopathological level. We found a statistically significant increase in collagen and elastic fiber thickness in areas received CO_2 laser either alone or combined by LGF, with better results in areas received combined therapy.

Our results came across the results of other studies that evaluated the effect of fractional CO_2 laser on SD and reported significant improvement in the clinical appearance with 10.600-nm CO_2 fractional laser.[2-4] Contrary to our results, Tehranchinia et al (2018)[12] assessed the effectiveness of fractional CO_2 laser 10 600 nm in striae alba and reported minimal improvement. They performed 2 sessions only and suggested that more sessions could be necessary to achieve better results. It has been reported that treatment result of fractional CO_2 laser could be amplified when combined with pulsed dye laser,[13] fractionated microneedle radiofrequency[14] and by succinylated atelocollagen.[7]

When comparing the effect of CO_2 laser with LGF, we reported a superior role of CO_2 laser over LGF similar to other comparative studies that compared the effect of CO_2 laser with other modalities. Naeini and Soghrati (2012)[15] showed that the improvement of

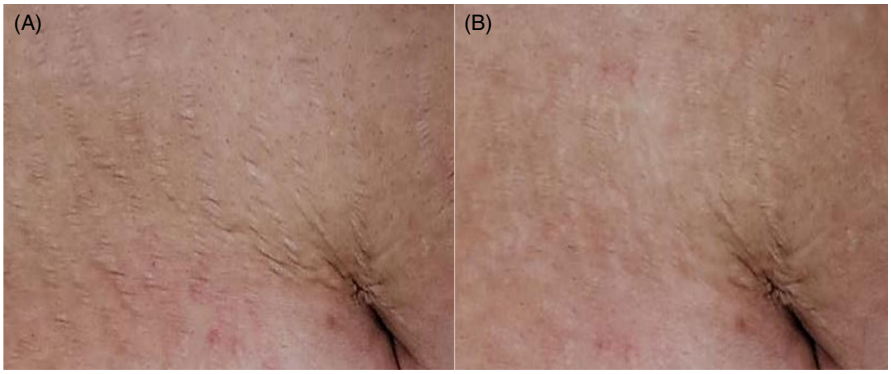

FIGURE 2 A, Clinical photography of a 39-year-old patient with striae alba on her abdomen due to pregnancy before treatment, and B, clinical photography of the same site showing marked improvement 6 wk after treatment with fractional CO_2 laser and LGF injection

fractional CO_2 laser treated SD was higher as compared with combined topical 10% glycolic acid and 0.05% tretinoin cream. Similarly, El Taieb and Ibrahim (2016)[16] stated that fractional CO_2 laser was superior to intense pulsed light for SD.

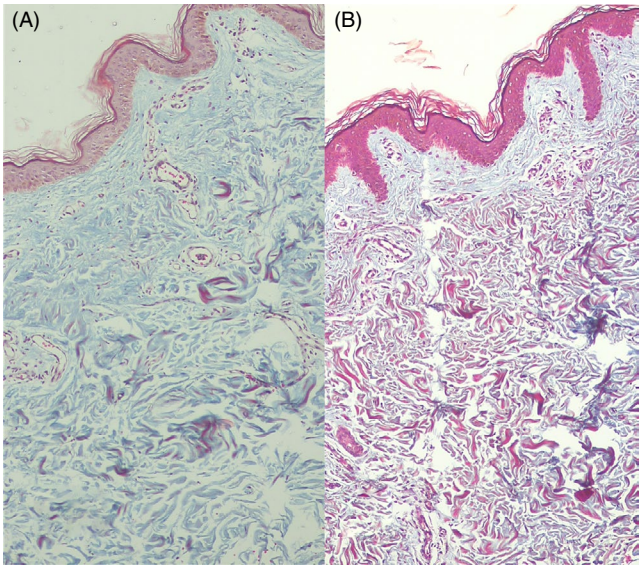

FIGURE 4 A, Pretreatment histopathologic photography (Masson trichrome stain, ×100 magnification) showing thinned, sparse, and fragmented collagen fibers. B, Histopathologic photography (Masson trichrome stain, ×100) showing regularly aligned, continuous, and thicker collagen fiber 6 wk after fractional CO_2 laser and LGF injection

We reported PIH in 40% of our cases in areas treated either by fractional CO_2 laser or by the combined therapy. All of those cases had skin type IV, and 62.5% of them had striae rubra. This could be related to the pulse duration or the dwell time (600 μs) and the laser power (18 watt) we used. Minimizing the pulse duration and additionally the laser power could have been safer for skin type IV. Additionally, we used the same laser parameters for all cases (striae alba and rubra). Therefore, we suggest using lower pulse duration and lower laser power in skin type IV especially in cases of striae rubra to minimize the risk of PIH that could be compensated by increasing number of sessions until reaching the desirable results. Yang and Lee (2011)[17] compared ablative fractional 10 600 nm CO_2 laser with non-ablative fractional 1550 nm Erbium glass laser in striae alba in Asian patients with skin type IV. They reported that although ablative fractional CO_2 laser gave better results, nevertheless, it was more painful and resulted in more PIH and longer post-treatment erythema. Nouri et al (1999)[18] acclaimed that laser treatment for SD should be avoided or used with caution in patients with skin types IV–VI due to risk of PIH development. Although the 585-nm pulsed dye laser has shown to improve striae rubra, but not striae alba, due to its affinity for hemoglobin, PIH could still be a significant complication after treatment of striae rubra with pulsed dye laser in skin types IV-VI.[19] Our results advocate fractional CO_2 laser for striae alba in skin type III more than in skin type IV but not for striae rubra due to high incidence of PIH.

In our study, we used LGF as a standardized form of conventional PRP that was developed by a patented method for growth factor preparation. Each LGF™ vial we used had a standard amount of

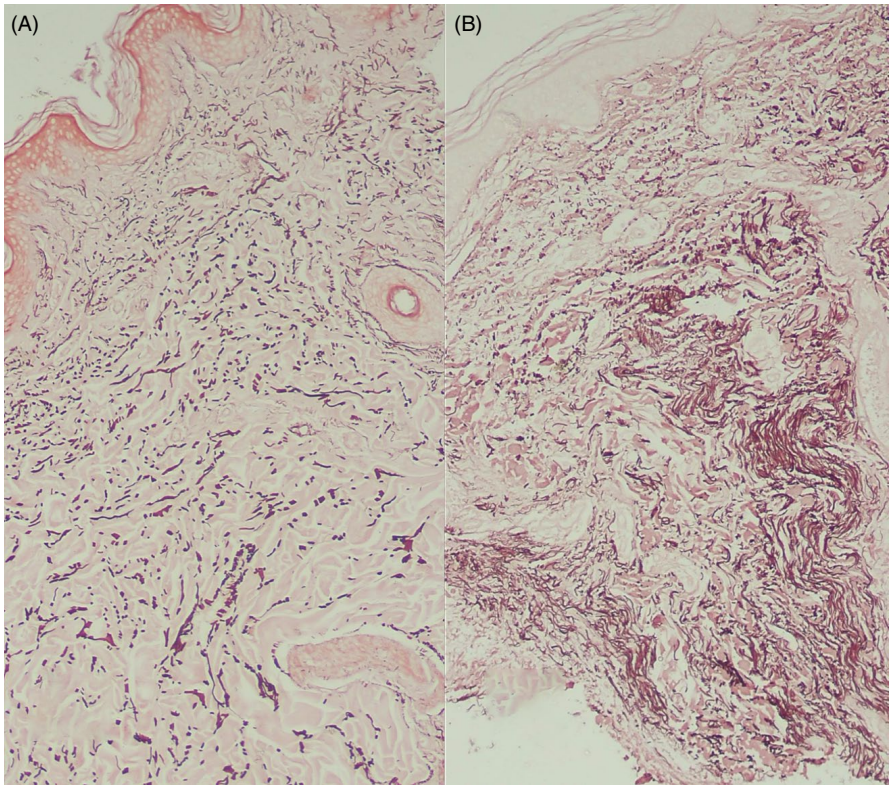

FIGURE 5 A, Pretreatment histopathologic photography (Orcein stain, ×100 magnification) showing few, unevenly distributed, thin, and fragmented elastic fibers. B, Histopathologic photography (Orcein stain, ×100) showing regular, longer, thicker elastic fibers that increased in number 6 wk after fractional CO_2 laser and LGF injection

TABLE 3 Comparison between studied areas regarding collagen fiber and elastic fiber thickness before and after treatment

Areas	Histologic variable	Statistical variable	Before treatment	After treatment	Paired *t* test	*P*-value
Area A	Collagen fiber thickness (μm)	Range	13.1-37.3	13.5-39.5	9.762	**.011**
		Mean ± SD	24.9 ± 7.1	28.6 ± 9.1		
	Elastic fiber thickness (μm)	Range	1.0-8.1	1.1-11.2	6.544	**<.001**
		Mean ± SD	2.88 ± 2.24	5.18 ± 2.96		
Area B	Collagen fiber thickness (μm)	Range	13.1-37.3	15.2-42.5	12.662	**.007**
		Mean ± SD	24.90 ± 7.12	29.94 ± 9.09		
	Elastic fiber thickness (μm)	Range	0.7-7.4	1.1-11.2	6.147	**.005**
		Mean ± SD	2.83 ± 1.97	5.18 ± 2.96		
Area C	Collagen fiber thickness (μm)	Range	13.1-37.3	13.5-31.7	0.167	.271
		Mean ± SD	24.9 ± 7.1	26.1 ± 4.7		
	Elastic fiber thickness (μm)	Mean ± SD	1.0-10.83	1.1-11.2	0.673	.194
		Range	4.79 ± 2.09	5.18 ± 2.96		

Significant *P*-values are indicated in bold.

TABLE 4 Comparison between studied areas regarding the mean difference in collagen and elastic fiber thickness

Histopathologic results	Area A	Area B	Area C	ANOVA *F*-ratio	*P*-value
Collagen fiber thickness (μm) Mean difference ± SD	3.7 ± 2	5.04 ± 1.97	1.2 ± 2.4	18.254	**<.001**
Elastic fiber thickness (μm) Mean difference ± SD	2.3 ± 0.72	2.32 ± 0.99	0.39 ± 0.87	12.332	**.042**

Note: Significant *P* values are in bold.

growth factors equivalent to those coming from 2 million platelets/μL. Angeliki et al (2015)[20] suggested that clinically appreciated PRP should contain at least platelet count of 10^6/μL. Kieb et al (2016)[10] developed a PRP powder (freeze-dried standardized growth factor preparation) and suggested that it would have advantages over conventional PRP. First, the defined concentrations of growth factors might overcome discrepancies associated with conventional PRP. Second, the in vitro stimulation of platelets during LGF preparation permits avoiding the use of thrombin or calcium injections in vivo. Additionally, and according to Marx (2004),[21] LGF have a much longer shelf life as compared to the autologous PRP (12-18 months vs 8 hours) that practically could be more easily to use. Accordingly, we hypothesized that LGF intralesional injection could have a good clinical impact on SD.

We reported that areas treated with LGF alone exhibited insignificant SD width reduction after treatment. Additionally, other clinical scores and histopathologic evaluation showed insignificant improvement in such areas as compared to areas either treated with CO_2 laser only or by combined therapy. It is worth mentioning that the response was not as high as we hypothesized and as expected based on studies on PRP in SD.[1,5] We attributed the low response to LGF we encountered to many factors. The number of platelets needed to achieve clinical results would have been more than the number we had used. Also, the number of sessions needed could be more than three sessions. Additionally, collagen deposition has been documented to continue after cessation of various aesthetic treatments for long periods[22] demanding longer follow-up periods. Furthermore, the inactivation of leukocytes during LGF preparation may have changed the cytokine milieu that might have a permissive effect with the growth factors on skin regeneration. Recently, Ahmed and Mostafa (2019)[23] advocated the therapeutic role of PRP in striae rubra but disputed its use in striae alba. This may further explain the minimal improvement in our cases received LGF only as most of our cases (75%) were striae alba. We did not perform comparative analysis regarding the type of striae and the degree of clinical and histopathologic improvement in all areas as it would be statistically weak due to small number of striae rubra. Further studies on a larger scale of cases with equal percentage of each type of SD would yield more reliable results.

We have shown that areas which received combined LGF injection after CO_2 laser exhibited the best clinical and histopathological results compared to areas treated with fractional CO_2 laser only. This verifies the additive or adjuvant role of LGF to fractional CO_2 laser in our study. Near enough to our results, Na et al (2011)[24] advocated that treatment with PRP after ablative

CO_2 fractional laser additively improves the appearance of SD as compared to the fractional CO_2 laser alone. We presumed that LGF might perform a boosting role on the laser-activated fibroblasts to maintain or augment their activation rather than initiating role for their activation. Similarly, PRP has been found to have synergistic effect with microdermabrasion[5] and radiofrequency[6] in SD treatment. Furthermore, Kadry et al (2018)[25] studied the effect of fractional CO_2 laser combined with PRP vs either fractional CO_2 laser alone or PRP alone in the treatment of nonsegmental vitiligo. They demonstrated that combined fractional CO_2 laser with PRP and sun exposure yielded the best result that was followed by the result of PRP alone and then the result of fractional CO_2 laser alone.

Using LGF in our study was potentially safe with minimal side effects in the form of mild pain at site of injection that last for few hours after the session. PRP had been reported to cause localized reactions such as inflammation at the injection site[26] that we did not encounter. The inactivation of leukocytes may have yielded LGF to be safer than PRP with no side effects.

In conclusion, fractional CO_2 yielded superior result over LGF in improving SD based on clinical and histopathologic results. The effect of fractional CO_2 was augmented by combination with LGF intralesional injection. The results of the current study did not recommend LGF as a monotherapy for SD. However, LGF is a novel therapy and further studies using different LGF preparations with different platelet numbers and growth factor concentrations could be tried with modulation of the number and spacing of sessions to accomplish the best SD improvement.

ACKNOWLEDGMENTS

The authors would like to thank the cooperation of the patients who accepted to be enrolled in the study.

CONFLICT OF INTEREST

None declared.

ORCID

Azza E. Mostafa https://orcid.org/0000-0003-0357-5558

REFERENCES

1. Hodeib AA, Hassan GFR, Ragab MNM, Hasby EA. Clinical and Immunohistochemical comparative study of the efficacy of carboxytherapy vs platelet- rich plasma in treatment of stretch marks. *J Cosmet Dermatol*. 2018;17:1008-1015.
2. Lee SE, Kim JH, Lee SJ, et al. Treatment of striae distensae using an ablative 10.600 nm carbon dioxide fractional laser: a retrospective review of 27 participants. *Dermatol Surg*. 2010;36:1683-1690.
3. Tabaie SM, Nasr E, Naderi MS, Rezvan M. Treatment of striae distensae using fractional ablative CO2 laser in skin types II-IV: a retrospective case series study. *J Cosmet Laser Ther*. 2018;20(6):330-334.
4. Cho SB, Lee SJ, Lee JE, Kang JM, Kim YK, Oh SH. Treatment of striae alba using the 10.600-nm carbon dioxide fractional laser. *J Cosmet Laser Ther*. 2010;12:118-119.
5. Ibrahim ZAES, El-Tatawy RA, El-Samongy MA, Ali DAM. Comparison between the efficacy and safety of platelet-rich plasma vs. microdermabrasion in the treatment of striae distensae: clinical and histopathological study. *J Cosmet Dermatol*. 2015;14:336-346.
6. Kim IS, Park KY, Kim BJ, Kim MN, Kim CW, Kim SE. Efficacy of intradermal radiofrequency combined with autologous platelet-rich plasma in striae distensae: a pilot study. *Int J Dermatol*. 2012;51:1253-1258.
7. Shin JU, Roh MR, Rah DK, Ae NK, Suh H, Chung KY. The effect of succinyl atedatelocollagen and ablative fractional resurfacing laser on striae distensae. *J Dermatolog Treat*. 2011;22:113-121.
8. Sobhi RM, Mohamed IM, El Sharkawy DA, El Wahab MAEFA. Comparative study between the efficacy of fractional micro-needle radiofrequency and fractional CO2 laser in the treatment of striae distensae. *Lasers Med Sci*. 2019;34:1295-1304.
9. Burnouf PA, Juan PK, Su CY, et al. A novel virally inactivated human platelet lysate preparation rich in TGF-beta, EGF and IGF, and depleted of PDGF and VEGF. *Biotechnol Appl Biochem*. 2010;56(4):151-160.
10. Kieb M, Sander F, Prinz C, et al. Platelet rich plasma powder: a new preparation method for the standardization of growth factor concentration. *Am J Sport Med*. 2016;45(4):954-960.
11. Fahmy HM. A method for preparing a growth factors containing platelet releasate. International publication number WO2018091713. https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2018091713. Accessed on 25/2/2020
12. Tehranchinia Z, Mahboubianfar A, Rahimi H, Saedi N. Fractionated CO_2 laser in the treatment of Striae alba in darker skinned patients - a prospective study. *J Lasers Med Sci*. 2018;9(1):15-18.
13. Naeini FF, Nikyar Z, Mokhtari F, Bahrami A. Comparison of the fractional CO2 laser and the combined use of a pulsed dye laser with fractional CO_2 laser in striae alba treatment. *Adv Biomed Res*. 2014;3:184.
14. Naeini FF, Behfar S, Abtahi-Naeini B, Keyvan S, Pourazizi M. Promising option for treatment of striae alba: fractionated microneedle radiofrequency in combination with fractional carbon dioxide laser. *Dermatol Res Pract*. 2016;2016:2896345.
15. Naeini FF, Soghrati M. Fractional CO_2 laser as an effective modality in treatment of striae alba in skin types III and IV. *J Res Med Sci*. 2012;17:928-933.
16. El Taieb MA, Ibrahim AK. Fractional CO_2 laser versus intense pulsed light in treating striae distensae. *Indian J Dermatol*. 2016;61:174-180.
17. Yang YJ, Lee GY. Treatment of striae distensae with nonablative fractional laser versus ablative CO_2 fractional laser: a randomized controlled trial. *Ann Dermatol*. 2011;23:481-489.
18. Nouri K, Romagosa R, Chartier T, Bowes L, Spencer JM. Comparison of the 585 nm pulse dye laser and the short pulsed CO_2 laser in the treatment of striae distensae in skin types IV and VI. *Dermatologic Surg*. 1999;25(5):368-370.
19. De Angelis F, Kolesnikova L, Renato F, Liguori G. Fractional nonablative 1540-nm laser treatment of striae distensae in Fitzpatrick skin types II to IV: clinical and histological results. *Aesthet Surg J*. 2011;31:411-419.
20. Angeliki G, Alexandros-Efstratios K, Dimitris R, Konstantinos K. Platelet-rich plasma as a potential treatment for noncicatricial alopecias. *Int J Trichol*. 2015;7(2):54-63.
21. Marx R. Platelet-rich plasma. Evidence to support its use. *J Oral Maxillofac Surg*. 2004;62(4):489-496.
22. Kruglikov IL. Neocollagenesis in non invasive aesthetic treatment. *J Cosmet Dermatol Sci Appl*. 2013;3:1-5.
23. Ahmed NA, Mostafa OM. Comparative study between: carboxytherapy, platelet-rich plasma, and tripolar radiofrequency, their efficacy and tolerability in striae distensae. *J Cosmet Dermatol*. 2019;18(3):788-797.

24. Na JI, Choi JW, Choi HR, et al. Rapid healing and reduced erythema after ablative fractional carbon dioxide laser resurfacing combined with the application of autologous platelet-rich plasma. *Dermatol Surg*. 2011;37:463-468.
25. Kadry M, Tawfik A, Abdallah N, Badawi A, Shokeir H. Platelet-rich plasma versus combined fractional carbon dioxide laser with platelet-rich plasma in the treatment of vitiligo: a comparative study. *Clin Cosmet Investig Dermatol*. 2018;11:551-559.
26. Mei-Dan O, Mann G, Maffulli N. Platelet-rich plasma: any substance into it? *Br J Sports Med*. 2010;44(9):618-619.

How to cite this article: Abdallah M, Fahmy H, Abdel Hameed S, Mostafa AE. Ablative fractional CO_2 laser vs lyophilized growth factor intralesional injection vs combination of both modalities for striae distensae treatment. *J Cosmet Dermatol*. 2020;00:1–9. https://doi.org/10.1111/jocd.13564