

# Clinical and immunohistochemical comparative study of the efficacy of carboxytherapy vs platelet-rich plasma in treatment of stretch marks

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## Summary

**Background:** Striae distensae are dermal scars with a linear atrophic depression. The exact origin of striae distensae remains unrevealed, but low expression of collagen and fibronectin genes in the affected tissue was found. Several treatment modalities have been proposed, yet no consistent modality is available.

**Aim of the work:** To evaluate and compare the efficacy and safety of carboxytherapy vs platelet-rich plasma (PRP) in treatment of stretch marks.

**Patients and methods:** This study included 20 patients with striae alba. Every patient received treatment in the form of PRP injection in their right side (group A) and carboxytherapy session in their left side (group B) every 3-4 weeks for 4 sessions. Skin biopsies were taken before and after treatment, and they were subjected to fibronectin immunohistochemical stain.

**Results:** There was a significant improvement in striae alba in both groups after than before treatment. There was no significant difference between both groups as regards either percentage of improvement, response (grading scale), or patient satisfaction. The fibronectin-stained area was significantly higher in both groups after than before treatment, and it was significantly higher after treatment in group (B) than group (A).

**Conclusions:** Both methods were safe and effective with minimal side effects. There was no significant difference between both methods of treatments. This was confirmed histopathologically by fibronectin expression which is found to be low in striae and increased significantly after treatment. But fibronectin expression was higher in group (B) than (A).

## KEYWORDS

carboxytherapy, platelet-rich plasma, striae alba

## 1 | INTRODUCTION

Stretch marks or striae are common skin condition occurring in both genders, but they are more prevalent among women. These are linear dermal scars that are accompanied by epidermal atrophy. They usually occur frequently in numerous physiological and pathological conditions, such as adolescent growth, pregnancy, obesity, Cushing disease, Marfan syndrome, and long-term systemic or topical steroid use. Decreased expression of collagen and fibronectin genes has also been associated with striae.<sup>1</sup>

Stretch marks are found in all races and are usually located on the buttocks, thighs, abdomen, knees, calves, and lumbosacral areas. Clinically, striae in early stage are pink or red in color (striae rubra) but over time and with atrophic changes, they become white (striae alba). The histopathological picture of striae is similar to scar, and development of striae is similar to wound healing or scar formation.<sup>2</sup>

Many therapeutic modalities have been tried including topical retinoid, microdermabrasion, radiofrequency, photothermolysis, intense pulsed light, ablative and nonablative laser, and fractional lasers, but no consistently effective modality is available yet.<sup>3</sup>

Carboxytherapy refers to the administration of CO<sub>2</sub> for therapeutic purposes.<sup>4</sup> It is used for the treatment of dark under-eye circles, stretch marks, cellulite reduction, and nonsurgical fat sculpting on the face and body. It increases oxygenated blood flow to the region injected. Carboxytherapy also increases collagen formation in the skin, giving it a better appearance. When CO<sub>2</sub> is injected subcutaneously, it diffuses at the cutaneous microcirculatory level. As a result, the body attempts to correct what it considers an imbalance of oxygen/carbon dioxide levels, increasing blood flow to supply oxygen and nutrients to the skin and vessels. This ultimately improves the appearance of the skin.<sup>5,6</sup> Carbon dioxide therapy is a relatively new indication for old white stretch marks. It works in different ways: Neo-angiogenesis below the mark, which adds a pink color, increases oxygen in the tissues and collagen synthesis, which reduce the creased appearance.<sup>6</sup>

Platelet-rich plasma (PRP) represents a new biotechnology that is part of the growing interest in tissue engineering and cellular therapy today. By definition, PRP is an autologous preparation of platelets in concentrated plasma. Although the optimal PRP platelet concentration is unclear, the current method by which PRP is prepared reported 300%-700% enrichment, with high platelet concentrations. Owing to this high concentration of growth factors, PRP has attracted attention in the field of dermatology.<sup>7</sup> PRP is a common treatment nowadays in the cosmetic dermatological field. It is used in treatment of stretch marks as it stimulates fibroblasts within the skin to produce collagen fibers. As PRP is made from one's self-blood, the treatment is regarded as safe and inexpensive.<sup>8</sup>

### 1.1 | Aim of the works

The aim of this study was to evaluate and compare the efficacy and safety of carboxytherapy vs PRP in treatment of stretch marks.

## 2 | PATIENTS AND METHODS

### 2.1 | Random blind study

After approval of the research ethics committee of Tanta Faculty of Medicine (approval code 30401/06/15), this study was carried out on 20 patients with bilateral striae alba, recruited from the Out-Patient Clinic of Dermatology and Venereology Department, Tanta University Hospitals, during the period from June 2015 to September 2016. Inclusion criteria were newly diagnosed cases that were otherwise clinically free and not receiving treatment for striae alba in the last 6 weeks and patients who accepted to be enrolled in the study and signed informed consents. Patients with history of keloidal scarring, bleeding and coagulation disorders, patients with respiratory insufficiency, renal failure, chronic congestive heart failure, liver disorders, and severely anemic patients, also pregnant and lactating females, were excluded from the study. All patients were subjected to complete history taking, thorough general examination to exclude any systemic diseases, full dermatological examination. An informed consent was taken from all patients after full explanation of the procedure, risks, and purpose of the study. Investigations were carried out for exclusion of any abnormalities such as pregnancy test for female patients, complete blood count, bleeding and coagulation time, and liver and renal function tests.

Every patient received treatment in the form of PRP injection session every 3-4 weeks in right side (group A) and carboxytherapy session every 3-4 weeks in left side (group B) of the same affected site in the same patient, for 4 sessions each. Skin biopsies were taken before treatment and after completion of sessions to assess clinical results and to compare the results of both sides. The specimens were processed and subjected to ordinary hematoxylin and eosin (H&E) stains and to fibronectin immunohistochemical stain. The patients were followed up for 3 months after the last session.

### 2.2 | Group A

Ten to 20 cc of venous blood had been collected under complete aseptic condition. The whole blood sample was collected into tubes containing sodium citrate (10:1) as an anticoagulant. The citrated whole blood was subjected to 2 centrifugation steps. The initial centrifugation was performed (soft spin) at 1409 g for 7 minutes to separate the plasma and platelets from the red and white cells. The resulting plasma supernatant, which contained the suspended platelets, was harvested to a second centrifugation step (hard spin) at 2504 g for 5 minutes, leading to separation of the plasma into 2 portions: PPP (platelet poor plasma) and PRP. The lower 1-2 cc of the plasma was yielded as PRP concentrate after centrifugation. Topical anesthetic cream was applied to the treated area, and

0.1 cc of PRP was injected per point with insulin syringe subcutaneously with a space of 1 cm in between different points of injections.<sup>9</sup>

### 2.3 | Group B

Patients underwent subcutaneous injections of CO<sub>2</sub>. The instrument used was carboxytherapy device (Concerto SN: CO 501-0600. Italy). Topical anesthetic cream was applied to the treated area. A 30-G needle was used for injection. Total amount of gas was administered equal to 100 mL with flow rate 80-150 cc/min. The average time for each session was between 10 and 15 minutes. External compression was avoided, as it may accelerate the leakage of gas through the skin.<sup>10</sup>

### 2.4 | Assessment of the efficacy of the therapeutic procedure after completing all sessions

#### 2.4.1 | Clinical assessment

Photographs were taken at baseline and before each session; then, photographs were taken after 3 months of last session for follow-up. Three dermatologists were asked to record percentage of improvement for each patient after completion of the treatment by comparing before and after digital photographs. The quartile grading scale was as follows<sup>11</sup>: No improvement in SD: if improvement was 0%. Mild improvement: 0%-25% improvement. Moderate improvement: 26%-50% improvement. Marked improvement: 51%-75% improvement. Excellent improvement: 76%-100% improvement. Each patient was asked at final visit about his/her satisfaction according to whether the patient was unsatisfied, slightly satisfied, satisfied, or very satisfied.

#### 2.4.2 | Histological assessment

Four millimeter punch biopsies were taken from the same lesional sites before treatment, after 3 months after treatment to detect the histopathological changes. They were stained by hematoxylin and eosin stains and fibronectin immunohistochemical stain. Immunohistochemical staining<sup>12</sup> was performed on formalin-fixed, paraffin-embedded, 4  $\mu$  sections from patient samples. The sections were deparaffinized, rehydrated, treated in microwave in sodium citrate (PH 6.0) for antigen retrieval, and washed with phosphate-buffered saline (PBS). Afterward, an incubation for 60 minutes was performed in a humidity chamber with mouse monoclonal primary antibodies against fibronectin (Catalogue # NBP2-22113 at 1:200 dilution; Novus Biological, USA) which was performed at room temperature. Sections were then covered with 4-5 drops of UltraVision biotinylated goat anti-polyvalent secondary antibody, incubated at room temperature for 10 minutes, then washed in PBS, followed by incubation with streptavidin peroxidase solution for 10 minutes at room temperature, and then rinsed with PBS. Streptavidin peroxidase solution was added for 10 minutes at room temperature and then rinsed

with PBS. Sections were then covered for 15 minutes by adding 1 drop of 3,30-diaminobenzidine tetrahydrochloride (DAB) chromogen mixed with 2 mL of DAB substrate. Finally, sections were counterstained with Mayer's hematoxylin, dehydrated in alcohol, and mounted in distyrene, plasticizer, and xylene (DPX). Negative controls had primary antibody replaced by buffer.

For each stained section in the study groups, multiple images were taken by Leica DM500 microscope with built-in Leica ICC50 digital camera. Images were then entered into Image J image analyzing system version # 1.50d. The region of interest was determined by defining our selection on selected RGB stalk and then adjusting the threshold in comparison with the original image. Measurements were limited to threshold and set to area, area fraction (percentage). The mean area percentage of staining of multiple images from the same section was then calculated.

### 2.5 | Statistical analysis of the data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0 for Microsoft Windows; SPSS Inc., Chicago, IL, USA. Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum), mean, standard deviation, and median. The significance of the obtained results was judged at the 5% level. The used tests were marginal homogeneity test (to analyze the significance between the different stages), paired *t* test (it is used for normally quantitative variables and to compare between 2 periods), and Pearson coefficient test (to correlate between 2 normally quantitative variables).<sup>13</sup>

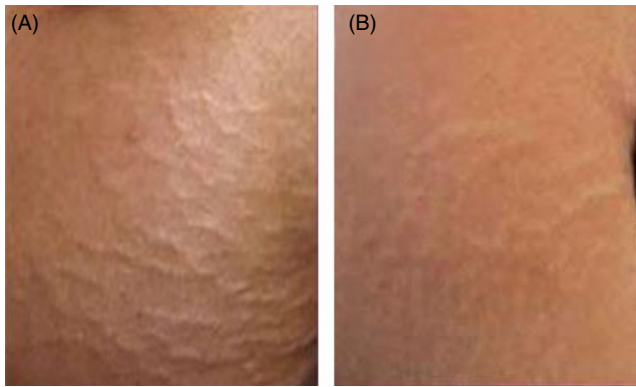
## 3 | RESULTS

This study included twenty patients with bilateral striae alba. The patients included 14 females (70%) and 6 males (30%). Their ages ranged from 17 to 40 years with a mean  $\pm$  SD 25.55  $\pm$  6.24. The duration of the disease ranged from 1 to 8 years with a mean  $\pm$  SD 3.90  $\pm$  2.27. According to the site of striae alba, it involved the arms in 4 patients (20%), the abdomen in 10 patients (50%), the shoulders in 2 patients (10%), the thighs in 2 patients (10%), and the breasts (10%) in 2 patients. The study included 5 patients (25%) with skin type III and 15 patients (75%) with skin type IV.

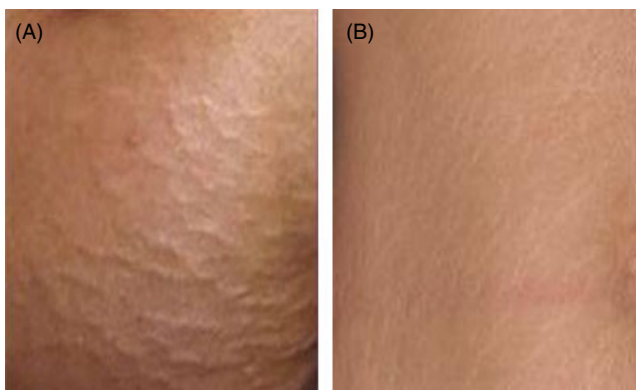
### 3.1 | Evaluation of the efficacy of therapeutic procedure

#### 3.1.1 | Group A (the right side of the involved site, treated with PRP injection sessions)

The percentage of improvement ranged from 20% to 80% with a mean  $\pm$  SD 44.50  $\pm$  18.15. The response of treatment (grading scale) was mild in 4 patients (20%), moderate in 10 patients (50%), marked in 5 patients (25%), and excellent in only 1 patient (5%).



**FIGURE 1** A, Patient with striae alba in the abdomen before treatment. B, After platelet-rich plasma sessions showing marked improvement



**FIGURE 2** A, Patient with striae alba in the abdomen before treatment. B, After carboxytherapy sessions showing excellent improvement

Also, all patients were asked about their satisfaction. Two patients (10%) were very satisfied, 8 patients (40%) were satisfied, 6 patients (30%) were slightly satisfied, and 4 patients (20%) were unsatisfied (Figure 1).

### 3.1.2 | Group B (the left side of the same involved site in the same patient, treated with carboxytherapy injection sessions)

The percentage of improvement ranged from 20% to 80% with a mean  $\pm$  SD 48.50  $\pm$  18.45. The response of treatment (grading scale) was mild in 3 patients (15%), moderate in 12 patients (60%), marked in 3 patients (15%), and excellent in 2 patients (10%). Three patients (15%) were very satisfied, 7 patients (35%) were satisfied, 5 patients (25%) were slightly satisfied, and 5 patients (25%) were unsatisfied (Figure 2).

### 3.1.3 | Comparison between both groups

There was no significant difference between both groups regarding either percentage of improvement (but the mean of improvement in group B was higher than A), response (grading scale), or patient satisfaction (Table 1).

Regarding the reported side effects of both procedures, they were minimal and tolerated in both groups as in group (A): Ecchymosis was found in 40% of patients and pain during injection in 50%, and in group (B): ecchymosis in 45% and pain in 45% with no significant difference between both groups. Pain was temporary and limited to the time of injection and ecchymosis resolved within 3-4 days. No postoperative hyperpigmentation was reported even in the skin type IV.

	Group (A) (n = 20)		Group (B) (n = 20)		Test of sig.	P value
	No.	%	No.	%		
Percentage of improvement %						
Min.-Max.	20-80		20-80		$t = 0.965$	.347
Mean $\pm$ SD	44.50 $\pm$ 18.15		48.50 $\pm$ 18.45			
Median	40		50			
Response (grading scale)						
Mild (0%-25%)	4	20	3	15	$MH\chi^2 = 0.378$	.728
Moderate (26%-50%)	10	50	12	60		
Marked (51%-75%)	5	25	3	15		
Excellent (>75%)	1	5	2	10		
Satisfaction						
Unsatisfied	4	20	5	25	$MH\chi^2 = 0.728$	.467
Slightly	6	30	5	25		
Satisfied	8	40	7	35		
Very satisfied	2	10	3	15		

**TABLE 1** Comparison between groups A and B according to different parameters

$MH\chi^2$ : Chi square for marginal homogeneity test t: Paired t test

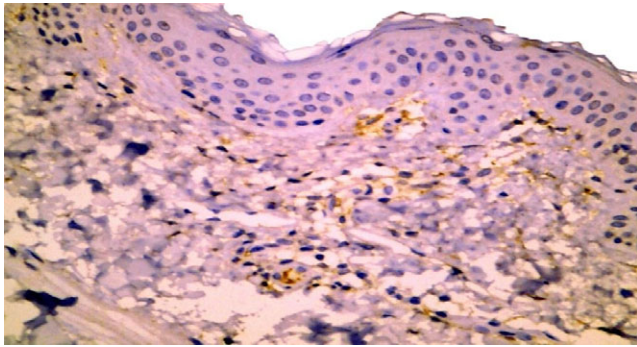
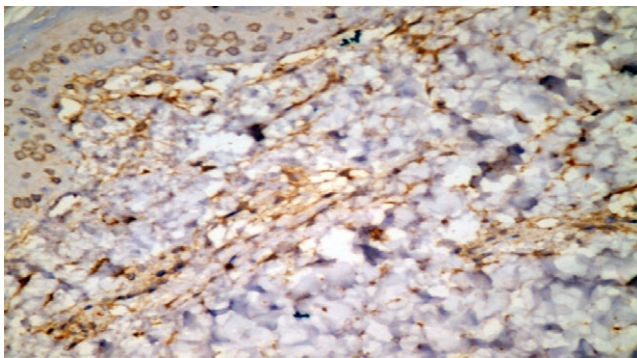
**TABLE 2** Fibronectin area percentage in both groups before and after treatment

	Before treatment for both sides	After treatment	
		Group (A) (n = 20)	Group (B) (n = 20)
FBN area%			
Min.-Max.	0.49-2.32	1.09-4.89	1.97 ± 5.28
Mean ± SD	1.13 ± 0.47	2.88 ± 1.10	3.65 ± 0.76
Median	1.05	3.05	3.76
$t_1$ ( $P_1$ )		10.689*( $<.001^*$ )	
$t_2$ ( $P_2$ )		7.460*( $<.001^*$ )	10.689*( $<.001^*$ )

$t_1$ ,  $P_1$ :  $t_1$  and  $P_1$  values for paired  $t$  test for comparing between right and left.

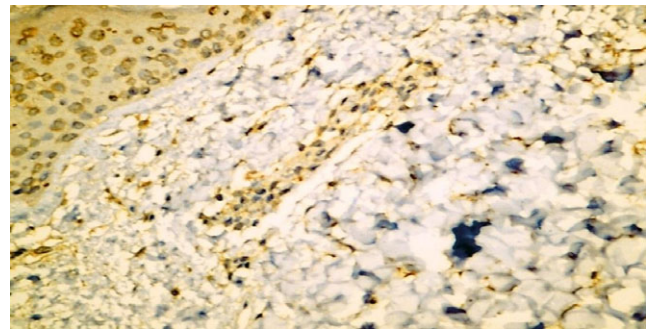
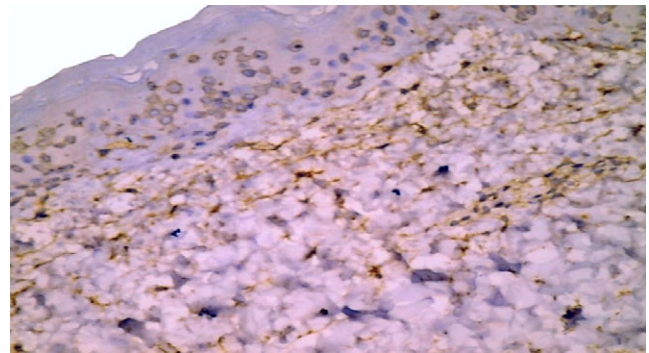
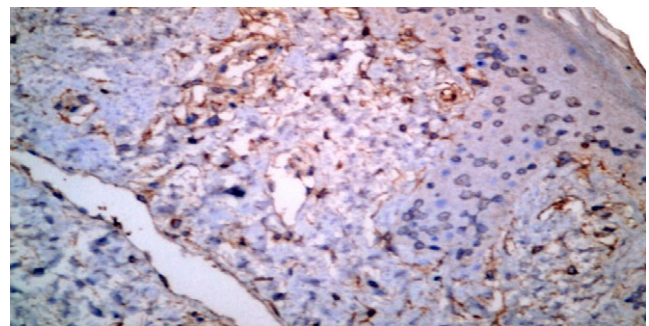
$t_2$ ,  $P_2$ :  $t_2$  and  $P_2$  values for paired  $t$  test for comparing between before and after.

\*Statistically significant at  $P \leq .05$ .

**FIGURE 3** Section from pretreated scar stained with fibronectin showing scattered weak expression in dermal fibrous tissue (Immunoperoxidase  $\times 400$ )**FIGURE 4** Section from postcarboxy-treated scar stained with fibronectin showing strong expression in dermal fibrous tissue and epidermal cytoplasm (Immunoperoxidase  $\times 400$ )

### 3.2 | Immunohistochemical results

Immunohistochemical staining for fibronectin and its evaluation using image J image analyzer to measure area percentage of stained area in the 2 studied groups revealed that mean area percentage of fibronectin expression in pretreated group ranged from 0.49 to 2.32 with

**FIGURE 5** Section from postcarboxy-treated scar stained with fibronectin showing moderate expression in dermal fibrous tissue and epidermal cells as well (Immunoperoxidase  $\times 400$ )**FIGURE 6** Section from post-platelet-rich plasma-treated scar stained with fibronectin showing moderate expression in large surface area in dermal fibrous tissue, especially around the vascular spaces (Immunoperoxidase  $\times 400$ )**FIGURE 7** Section from post-platelet-rich plasma-treated scar stained with fibronectin showing scattered strong expression in dermal fibrous tissue in larger surface area and epidermal cytoplasm (Immunoperoxidase  $\times 400$ )

mean  $\pm$  SD 1.13  $\pm$  0.47. After treatment, in group (A), it ranged from 1.09 to 4.89 with mean  $\pm$  SD 2.88  $\pm$  1.10, while in group (B) it ranged from 1.97 to 5.28 with mean  $\pm$  SD 3.65  $\pm$  0.76. The fibronectin-stained area was significantly higher in both groups after treatment when compared to fibronectin-stained area percentages before treatment. When comparing between both groups after treatment, the fibronectin-stained area was significantly higher in group (B) than group (A) ( $P < .001^*$ ) (Table 2, Figures 3-7).

**TABLE 3** Correlation between percentages of improvement in both groups with different parameters

	Percentage of improvement %			
	Group (A) Right side		Group (B) Left side	
	<i>r</i>	<i>P</i> value	<i>r</i>	<i>P</i> value
Sex	.215	.363	.285	.224
Age	.438	.054	.101	.673
Duration of striae	.178	.453	.036	.879
Response (grading scale)	.949*	<.001	.929*	<.001
Satisfaction	.322	.166	.637*	.003
FBN area % (before)	.236	.317	.188	.426
FBN area % (after)	.549*	.012	.503*	.024

*r*: Pearson coefficient.

\*Statistically significant at  $P \leq .05$ .

There was a positive significant correlation between the percentage of improvement and response (grading scale) in both groups. There was a significant positive correlation between the percentage of improvement and patient satisfaction in group (B) treated with carboxytherapy. There was a positive significant correlation between percentage of improvement and fibronectin-stained area after treatment in both groups with  $r = .504^*$ ,  $P = .021$  in group (A) and  $r = .544^*$ ,  $P = .012$  in group (B), respectively (Table 3). On the other hand, there were no significant correlations between percentage of improvement and either sex, age, duration, or site of lesions in both groups.

## 4 | DISCUSSION

Striae distensae (SD), also known as stretch marks, represent a cosmetically undesirable and very common problem difficult to be treated, especially in most healthy women.<sup>14</sup> Although SD does not cause any significant medical problems, they can be of great concern regarding their psychological implications, especially for females because of disfigurement. The exact pathogenesis of striae is still controversial. It may be due to changes in the components of ECM including fibrin, elastin, and collagen.<sup>15</sup> In the early stages of striae, there are sequential changes in elastolysis and mast cell degeneration. Elastic fibers are the primary target affected in striae, and then, the pathology extends to other dermal components.<sup>14</sup>

In this study, the age of patients ranged from 17 to 40 years. The higher ratio of patients was more than 20 years old (70%). This may be attributed to that SD is mostly due to puberty, pregnancy, and weight gain which occur usually around the age of twenties. This was in accordance with Kim et al.<sup>11</sup> Regarding gender, in the present study, 70% of them were females and 30% of the patients were males. The higher female-to-male ratio may be due to pregnancy, rapid gain, and loss of weight which are common in females. Larsson and Liden<sup>16</sup> also found female dominance in the prevalence of SD in a study of 8298 pupils in compulsory school.

According to clinical improvement in group A (PRP injection sessions), the degree of improvement in striae alba was excellent in only 5%, marked in 25%, moderate in 50%, and mild in 20%. None of the studied patients showed worsening of their lesions. Patients were asked about their satisfaction. They reported in 10% very satisfied, 40% satisfied, 30% slightly satisfied, and 20% unsatisfied.

The current results were similar to Kim et al.,<sup>11</sup> who conducted a study on 19 patients evaluating the efficacy of intradermal radiofrequency (RF) combined with autologous PRP in SD. PRP injections were performed using needle electrode of intradermal RF device in 3 sessions, 4 weeks interval. The results were assessed four weeks after the final session revealing that 5.3% of patients showed excellent improvement, 36.8% showed marked improvement, 31.6% patients showed moderate improvement, and 26.3% reported minimal improvement. None of the patients showed worsening of the SD. The patients' satisfactions were as follows: 15.8% very satisfied, 47.4% satisfied, 26.3% slightly satisfied, and 10.5% unsatisfied. Total of 63.2% of patients reported they were "satisfied" or "very satisfied" with the degree of overall improvement.

Suh et al.<sup>17</sup> treated SD by combination of enhanced penetration PRP and ultrasound after plasma fractional RF. Objective and subjective improvement scores were evaluated to demonstrate the efficacy. In the objective assessment, 71.9% of the participants reported "good" or "very good" overall improvement. In the subjective assessment, 72.2% of the participants reported "very satisfied" or "extremely satisfied" with overall improvement. The previous 2 studies<sup>11,17</sup> gave nearly similar results as the present study using PRP injection only revealing that PRP treatment is much simpler and cost-effective office technique compared with plasma fractional radiofrequency and acoustic wave pressure ultrasound, which are complicated and expensive procedures.

The results of the current study were in agreement with Ibrahim et al.,<sup>18</sup> who treated SD by intradermal injection of autologous PRP vs microdermabrasion sessions. The patients' satisfactions on treatment with PRP injection only were as follows: 30.4% very satisfied, 30.4% satisfied, 26.1% slightly satisfied, and 13% unsatisfied. According to the objective evaluation, 8.7% showed excellent improvement, 26.1% showed marked improvement, 30.4% showed moderate improvement, and 17.4% demonstrated mild improvement. They concluded that PRP alone was more effective than microdermabrasion alone in the treatment of SD, and better results were obtained when combining both procedures together.

Platelet-rich plasma contains various growth factors contained in alpha granules and dense granules. Alpha granules contain 7 fundamental growth factors: platelet degradation growth factor (PDGF- $\alpha$ , PDGF- $\beta$ ) which has been shown to be chemotactic to macrophages and fibroblasts, improve glycosaminoglycan and fibronectin deposition, transforming growth factor (TGF- $\beta$ 1 and 2), epidermal growth factor (EGF), fibroblast growth factor (FGF), and vascular endothelial growth factor (VEGF). These growth factors modulate cell proliferation, differentiation, angiogenesis, and chemotaxis. The dense granules contain bioactive factors including serotonin, histamine, dopamine, calcium, and adenosine. These bioactive factors can

increase membrane permeability and can modulate inflammation in the injected area to stimulate wound healing and new collagen formation.<sup>19</sup>

Furthermore, PRP is known to accelerate the generation of hyaluronic acid, which promotes cell proliferation and ECM synthesis and modulates the diameter of the collagen fibers and increases skin elasticity. It was found that activated PRP increases the expression of matrix metalloproteinase (MMPs), especially MMP-1. It facilitates the removal of damaged collagen fragments in the dermal matrix tissue, thus providing a better deposition of new collagen.<sup>20</sup>

According to clinical improvement in group B (carboxytherapy injection sessions), the degree of improvement in striae alba was excellent in 10%, marked in 15%, moderate in 60%, and mild in 15%. Patients' satisfactions revealed 15% very satisfied, 35% satisfied, 25% slightly satisfied, and 25% unsatisfied.

Pinheiro et al<sup>21</sup> compared the effects of carboxytherapy and RF on human skin. After 8 patients underwent abdominoplasty, each of them received a single treatment of carboxytherapy in 1 side and a single treatment of RF in the second side. Improvement as collagen remodeling was more evident and lasted longer with RF. However, carboxytherapy induces an increase in elastic fibers, while RF did not induce any alteration. These results proved that carboxytherapy leads to collagen remodeling and increases elastic fibers, so we used it in the present study in treating striae alba.

Carboxytherapy refers to the cutaneous and subcutaneous administration of CO<sub>2</sub> gas into dermal and subdermal structures. The body is triggered to increase the oxygen flow to the area injected and consecutively increase collagen formation.<sup>22</sup> The role of carboxytherapy in collagen remodeling is evidenced by the study of Paolo et al,<sup>23</sup> who tried this procedure in treatment of moderate-to-severe periorbital wrinkles and/or dark circles. At the end of the study period, patients reported a reduction in facial fine lines and wrinkles as well as a decrease in periorbital hyperpigmentation. Nach et al<sup>22</sup> stated that injection of the CO<sub>2</sub> gas has been used to improve stretch marks and skin laxity. It is believed that the mechanism of action for carboxytherapy is twofold. Initially, as the mechanical injection of the CO<sub>2</sub> gas causes destruction of fat cells and interruption of surrounding connective tissue, it has vasodilator effect that allows the accumulation of inflammatory response and enhances the process of healing, leading to increase collagen deposition and reorganization and eventual improvement in skin texture and tone.

Regarding the reported side effects of both procedures, they were minimal and tolerated in both groups as in group (A): Ecchymosis was found in 40% of patients and pain during injection in 50%, and in group (B): ecchymosis in 45% and pain in 45% with no significant difference between both groups. Pain was mild, temporary, and limited to the time of injection, and ecchymosis resolved within 3-4 days.

No postoperative hyperpigmentation was reported even in the skin type IV. The efficacy of treatment has not been affected by skin type, while other treatments such as pulsed dye laser and fractional photothermolysis cause postinflammatory hyperpigmentation,

especially in skin type IV. On comparing the results of PRP injection or carboxytherapy with laser therapy, it could be suggested that both methods gave moderate to marked results in SD over being safe, cost-effective, and less expensive than laser therapy with no postoperative hyperpigmentation.

According to the best of our knowledge, this was the first study performed to compare the efficacy of carboxytherapy and PRP in treating striae alba. The current study showed that there is no statistically significant difference between both carboxytherapy and PRP in treating striae alba, regarding either response (grading scale) or patient satisfaction. The percentage of improvement was found to be higher in group (B) but with no statistically significant difference. Using fibronectin as an indicator for improvement in striae is considered a reliable method as fibronectin expression is low in striae and it was found that it increased significantly after treatment than before treatment in both groups. Both methods induced significant fibronectin deposition in dermis. When comparing both groups after treatment, the fibronectin-stained area was significantly higher in group (B) than group (A), which was positively correlated with the clinical results (percentages of improvement).

It was concluded that both methods were effective in the treatment. The PRP method is cheap and is considered as a simple in-office technique needing no expensive devices with minimal tolerated side effects. On the other hand, carboxytherapy is an effective, safe, and novel method for the treatment of striae needing further researches. Nevertheless, expensive treatment sessions may be a limiting factor for such method. Additional studies are recommended on a larger number of patients to get better evaluations, and trials combining both methods may give better results. More sessions to be carried out for excellent results for both carboxytherapy and PRP will be valuable.

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## REFERENCES

1. Dover JS, Rothaus K, Gold MH. Evaluation of safety and patient subjective efficacy of using radiofrequency and pulsed magnetic fields for the treatment of striae. *J Clin Aesthet Dermatol.* 2014;7:30-33.
2. Naein FF, Soghrati M. Fractional CO<sub>2</sub> laser as an effective modality in treatment of striae alba in skin types III and IV. *J Res Med Sci.* 2012;17:928-933.
3. Gungor S, Sayilgan T, Gokdemir G, Ozcan D. Evaluation of an ablative and non-ablative laser procedure in the treatment of striae distensae. *Indian J Dermatol Venereol Leprol.* 2014;80:409-412.
4. Georgia SKL. Carbon dioxide therapy in treatment of cellulite: an audit of clinical practice. *Aesthetic Plast Surg.* 2010;34:239-243.
5. Ferreira LM, Silva EK, Jaimovich CA, et al. Carboxytherapy: seeking evidence for its use in plastic surgery and dermatology. *Rev Bras Cir Plast.* 2012;27:350-351.
6. Brandi C, D'Aniello C, Grimaldi L, et al. Carbon dioxide therapy: effects on skin irregularity and its use as a complement to liposuction. *Aesthetic Plast Surg.* 2004;28:222-225.

7. Marwah M, Godse K, Patil S, Nadkarni N. Is there is sufficient research data to use platelet-rich plasma in dermatology? *Int J Trichology*. 2014;6:35-36.
8. Fukaya M, Ito A. A new economic method for preparing platelet-rich plasma. *Plast Reconstr Surg Glob Open*. 2014;2:162.
9. Dhurat R, Sukesh M. Principles and methods of preparation of platelet rich plasma: a review and author's perspective. *J Cutan Aesthet Surg*. 2014;7:189-197.
10. Zenker S. Carboxytherapy, carbon dioxide injections in aesthetic medicine. *Prime Europe*. 2012;2:42-50.
11. 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.
12. Ganceviciene R, Böhm M, Fimmel S, Zouboulis CC. The role of neuropeptides in the multifactorial pathogenesis of acne vulgaris. *Dermatoendocrinol*. 2009;1:170-176.
13. Kotz S, Balakrishnan N, Read CB, Vidakovic B. *Encyclopedia of Statistical Sciences*. 2nd edn. Hoboken, NJ: Wiley-Inter science; 2006.
14. Stamatias GN, Lopes-DaCunha A, Nkengne A, Bertin C. Biophysical properties of Striae Distensae evaluated in vivo using non-invasive assays. *Skin Res Technol*. 2015;21:254-258.
15. Lee KS, Rho YJ, Jang SI, Suh MH, Song JY. Decreased expression of collagen and fibronectin genes in striae distensae tissue. *Clin Exp Dermatol*. 1994;19:285-288.
16. Larsson PA, Lidén S. Prevalence of skin diseases among adolescents 12-16 years of age. *Acta Derm Venereol*. 1980;60:415-423.
17. Suh DH, Lee SJ, Lee JH, Kim HJ, Shin MK, Song KY. Treatment of striae distensae combined enhanced penetration platelet-rich plasma and ultrasound after plasma fractional radiofrequency. *J Cosmet Laser Ther*. 2012;14:272-276.
18. Ibrahim ZA, El-Tatawy RA, El-Samongy MA, Ali DA. 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.
19. Leo MS, Kumar AS, Kirit R, Konathan R, Sivamani RK. Systematic review of the use of platelet-rich plasma in aesthetic dermatology. *J Cosmet Dermatol*. 2015;14:315-323.
20. Cho JW, Kim SA, Lee KS. Platelet-rich plasma induces increased expression of G1 cell cycle regulators, type I collagen, and matrix metalloproteinase-1 in human skin fibroblasts. *Int J Mol Med*. 2012;29:32-36.
21. Pinheiro NM, Crema VO, Millan BM, Carvalho AF, Mendonça AC. Comparison of the effects of carboxytherapy and radiofrequency on skin rejuvenation. *J Cosmet Laser Ther*. 2015;17:156-161.
22. Nach R, Zandifar H, Gupta R, Hamilton JS. Subcutaneous carboxytherapy injection for aesthetic improvement of scars. *Ear Nose Throat J*. 2010;89:64-66.
23. Paolo F, Nefer F, Paola P, Nicolò S. Periorbital area rejuvenation using carbon dioxide therapy. *J Cosmet Dermatol*. 2012;11:223-228.

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