

Efficacy and safety of carboxytherapy for treatment of striae: a clinical trial study

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Background: Striae is a common condition that is relatively difficult to treat. Recently, carboxytherapy was proposed as a treatment modality. This study aimed to evaluate the therapeutic effect of carboxytherapy in patients with striae.

Methods: This was a pilot clinical study. Patients were treated with 10 sessions of carboxytherapy every week. The patients were photographed at the onset of the treatment course, before each treatment session, and three months after the last ones. Two dermatologists compared the images of each patient before and three months after treatment and evaluated the treatment response based on the following scores: I, no improvement (0%); II, poor (1% to 25%); III, fair (26% to 50%); IV, good (51% to 75%); and V, excellent improvement (76% to 100%). Furthermore, patients' satisfaction with therapy outcome was recorded on a scale of 0 to 10.

Results: 15 patients were enrolled in this study; 2 (13.4%) were male and 13 (86.6%) were female. Three patients (20%) showed good response, one (6.7%) had a relatively good response, two showed (13.3%) poor response, and seven (46.6%) had no response to treatment. Analysis of the association of carboxytherapy outcome with different patients' characteristics showed no statistically significant correlation ($P > 0.05$).

Conclusions: Although carboxytherapy therapy did not result in a significant response in the majority of our patients, it is somehow capable of improving the striae in some patients. Further studies with bigger sample sizes may be required to ensure the efficacy of this modality in the treatment of striae.

Keywords: Striae distensae, carbon dioxide, clinical trial

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INTRODUCTION

Striae are common in all age groups, defined as linear atrophic depressions in injured dermis areas formed due to the protraction of skin. This condition is associated with different physiologic states including puberty, pregnancy, sudden growth or weight gain, sudden weight loss, obesity, and hypercortisolism. Striae usually develop at

between 5 to 50 years of age and are two times more common in women than men. Effective factors in striae formation are not completely understood, though this condition may be regarded as a reflection of deficiency in connective tissue, which leads to dermal atrophy. Several factors including hormones, mechanical stress, and genetic disposition are thought to be effective in striae formation ¹. Striae initially present as red to purple

lines with mild pruritus, which are called striae rubra. As time passes, these lines lose their color and become atrophic lesions called striae alba. Striae alba usually persist; however, they may fade with time. Striae are usually only an aesthetic concern but can also become ulcerated. Currently, no definitive treatments are available for striae, and affected people are usually disturbed by the appearance of these lesions.

Carboxytherapy is the transcutaneous administration of carbon dioxide (CO₂) for therapeutic purposes. Since Brandi and colleagues showed its efficacy in treating regional obesity (a significant reduction in the abdomen, thigh, and knee circumference)², the use of carboxytherapy has attracted a lot of attention worldwide. Moreover, they also reported histologic changes supporting the efficacy of CO₂ injection in decreasing the subcutaneous fat layer and increasing the elasticity of the skin after liposuction². Due to the interaction between CO₂ and blood flow-regulating agents, carboxytherapy affects the microcirculation at the level of arterioles and meta-arterioles, causing increased tissue blood flow and increased lymphatic drainage. This enhancement of tissue nourishment results in enhanced wound healing. Changes in pH and improvement of metabolism cause temporary vasodilation and the creation of collateral vessels, leading to the reconstruction of intradermal collagen, thus improving the tonicity and appearance of the skin³. In striae alba, this leads to increased blood flow and restoration of hemoglobin, while reducing inflammation in the striae rubra.

Carboxytherapy is relatively safe and has turned into an attractive minor procedure. Side effects include mild pain, ecchymosis, and a regional crackling or burning sensation⁴. In recent years, the efficacy of carboxytherapy has been shown in multiple medical diseases and in the field of modern aesthetics. This procedure helps reduce the signs of aging and correct various beauty defects. It is also used in the treatment of cellulitis as well as acne scars, psoriasis plaques, eczema, scars in general, and burns; it has also been employed in improving circulation and wound healing and inhibiting inflammation^{4,5}.

In patients affected with striae, various treatments are used with different efficacies and adverse effects. Carboxytherapy is a non-invasive procedure

used for the treatment of striae that has shown promising results in various studies. Considering the importance of efficient treatment for patients with skin striae, the available evidence is not sufficient to support the efficacy of carboxytherapy for these patients. Therefore, in this study, we aimed to perform a clinical trial to evaluate the therapeutic effects of carboxytherapy in patients with skin striae.

MATERIALS AND METHODS

We designed a prospective clinical trial (IRCT20140414017271N3) to assess the efficiency of carboxytherapy in patients with skin striae rubra or alba who referred to the dermatology clinic of Imam Reza and Ghaem hospitals in Mashhad, Iran. Due to a lack of a similar study, we carried out a pilot study on 15 patients. After explaining the study to the patients, they provided written informed consent and were enrolled (Ethics committee code: IR.MUMS fm.REC.1396,360).

Inclusion and exclusion criteria

We included all patients who had striae and requested treatment. We excluded patients who did not consent to photography, did not return for follow-up, had severe anemia, respiratory, renal, or heart failure, had acute inflammation or other skin lesions in the location of CO₂ injection, had uncontrolled diabetes, mental weakness, or epilepsy, were pregnant or lactating, or were receiving carbonic anhydrase inhibitors such as acetazolamide.

Method of carboxytherapy

Ten sessions of carboxytherapy were performed across one-week intervals for each patient. The treatment area was first disinfected and CO₂ was injected subcutaneously using the 27 gauge needle and the ocotillo device (Exon) with a pressure of 30 kPa and a volume of 5 ml per injection.

Data collection

Initially, the skin of participants was examined and their basic characteristics including age, weight, family history of striae, skin type, type

(rubra versus alba) and duration of striae, and the number of pregnancies were recorded in a checklist. The method of the study included a before and after evaluation protocol, meaning that each patient was his or her control. Patients chose their treatment area and received 10 sessions of carboxytherapy across weekly intervals. At the beginning of the treatment and before the start of each session, the patients were photographed with a digital camera with the same settings in terms of angle, distance, and lighting. Moreover, the patients were again photographed three months after the cessation of treatment. At the end of the study, two dermatologists who were unaware of the study method compared patients' photos before the start of treatment and three months after the treatment and scored the patients as I: no improvement (0%), II: poor (1% to 25%), III: fair (26% to 50%), IV: good (51% to 75%), or V: excellent improvement (76% to 100%). Furthermore, patients' satisfaction with therapy outcome was recorded on a scale of zero to 10.

Statistical analysis

Quantitative data were presented as mean \pm standard deviation. The normality of distribution was evaluated using the Kolmogorov-Smirnov test. In order to assess the relationship between different variables, the chi-squared test was used for qualitative data, while the T-test and Mann-Whitney U test were used when appropriate for quantitative data. Data analysis was done using SPSS version 16 and a p-value of less than 0.05 was considered statistically significant.

RESULTS

This pilot study was done on 15 patients (13 females and 2 males) with striae. The mean age of participants was 36.7 years. All of our patients had a family history of striae. The most common reason for striae was puberty, followed by pregnancy. 12 patients had striae alba and three patients had striae rubra. The most common site of striae was the thighs followed by the abdomen. After carboxytherapy, 7 patients (46.6%) had no improvement, while 4 patients (26.6%) had a poor response, 1 patient (6.7%) showed a fair response, and 3 patients (20 %) had a good response. None

Table 1. Patient characteristics.

Age (years)	10.8 \pm 36.7
Sex	
Male	2 (13.4%)
Female	13 (86.6%)
Skin type (Fitzpatrick's classification)	
2	5 (33.3%)
3	6 (40%)
4	4 (26.7%)
Family history	
Positive	15 (100%)
Negative	0 (0%)
Cause of striae	
Puberty	7 (46.6%)
Pregnancy	4 (26.6%)
Weight gain	2 (13.3%)
Stretching	2 (13.3%)
Type of striae	
Rubra	3 (20%)
Alba	12 (80%)
Location of striae	
Arm	2 (13.3%)
Thigh	6 (40%)
Inguinal	1 (6.6%)
Abdomen	4 (26.7%)
Supraclavicular	1 (6.6%)
Calf	1 (6.6%)
Response to carboxytherapy †	
No improvement	7 (46.6%)
Poor improvement	4 (26.6%)
Fair improvement	1 (6.6%)
Good improvement	3 (20%)
Excellent improvement	0 (0%)

† Response to therapy was classified according to the percentage of recovery three months after the treatment compared to before starting the treatment as follows: no improvement (0%), poor (1% to 25%), fair (26% to 50%), good (51% to 75%), and excellent improvement (76% to 100%).

of our patients showed an excellent response to carboxytherapy (Table 1).

Moreover, we analyzed the association of response to therapy with different patient characteristics. Response to therapy was not correlated with age, sex, skin type and cause, type, location and duration of striae, and patients' satisfaction (Table 2). We did not include a family history of striae in this analysis since all of our patients had a positive family history of striae.

DISCUSSION

Striae is an aesthetic problem that psychologically affects patients. Despite various improvements in the field of dermatology and aesthetic medicine,

Table 2. Association between response to carboxytherapy and different patient characteristics.

	Response to carboxytherapy †					P-value
	No improvement	Poor improvement	Fair improvement	Good improvement	Excellent improvement	
Age (yrs)	35 ± 8.4	38.7 ± 17.8	32 ± 0	39.6 ± 8.9	-	0.076
Sex						
Male	0 (0%)	2 (100%)	0 (0%)	0 (0%)	0 (0%)	0.222
Female	7 (53.8%)	2 (15.4%)	1 (7.7%)	3 (23.1%)	0 (0%)	
Skin type						
2	1 (20%)	0 (0%)	1 (20%)	3 (60%)	0 (0%)	0.727
3	1 (16.7%)	0 (0%)	2 (33.3%)	3 (50%)	0 (0%)	
4	1 (25%)	1 (25%)	1 (25%)	1 (25%)	0 (0%)	
Cause of striae						
Puberty	4 (57.1%)	1 (14.3%)	1 (14.3%)	1 (14.3%)	0 (0%)	0.466
Pregnancy	2 (50%)	1 (25%)	0 (0%)	1 (25%)	0 (0%)	
Weight gain	1 (50%)	0 (0%)	0 (0%)	1 (50%)	0 (0%)	
Stretching	0 (0%)	2 (100%)	0 (0%)	0 (0%)	0 (0%)	
Type of striae						
Rubra	1 (33.3%)	0 (0%)	1 (33.3%)	1 (33.3%)	0 (0%)	0.852
Alba	2 (16.7%)	1 (8.3%)	3 (25%)	6 (50%)	0 (0%)	
Location of striae						
Arm	1 (50%)	0 (0%)	0 (0%)	1 (50%)	0 (0%)	0.507
Thigh	4 (66.7%)	1 (16.6%)	1 (16.6%)	0 (0%)	0 (0%)	
Inguinal	0 (0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	
Abdomen	2 (50%)	0 (0%)	1 (25%)	1 (25%)	0 (0%)	
Supraclavicular	0 (0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	
Calf	0 (0%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)	
Duration of striae (days)	131.1 ± 88.1	140 ± 107	100 ± 0	133.3 ± 40.4	0 (0%)	0.09
Patients' satisfaction ‡	1.1 ± 1.9	4 ± 4.6	2 ± 0	4.3 ± 3.7	0 (0%)	0.055

† Response to therapy was classified according to the percentage of recovery three months after the treatment compared to before starting the treatment as follows: no improvement (0%), poor (1% to 25%), fair (26% to 50%), good (51% to 75%), and excellent improvement (76% to 100%).

‡ Patients' satisfaction with the therapeutic outcome was recorded on a scale of 0 to 10.

striae remain difficult to treat. Several treatment options are available such as chemical peelings, mesotherapy, platelet-rich plasma, radiofrequency procedures, intense pulsed light, and laser ablations ⁶.

As a non-toxic gas, CO₂ can be introduced to the tissues via different methods of carboxytherapy. This substance interacts with water molecules, leading to a decrease in pH. Based on Bohr's law, at lower pH, hemoglobin has a lower tendency to bind with oxygen, meaning that oxygen is released. At a pH of 6.5, the permeability of the vascular wall is decreased, while the elasticity of collagen fibers decreases and their rigidity increases. Carbonic acid is divided into H and HCO₃, leading to the production of NaHCO₃, KHCO₃, and CaHCO₃, which increase the pH. An increase in the pH has a spasmolytic effect, decreasing the tonicity of capillaries and arterioles and leading to enhanced nourishment in the therapy location ⁷.

Carboxytherapy is a relatively new modality in the treatment of striae and a handful of reports are available that assess its efficacy. Padgorna *et al.* assessed the effects of carboxytherapy in patients with striae ⁸. Their results showed that carboxytherapy can reduce stretch marks by improving skin elasticity through the remodeling of collagen and elastin fibers, as shown by cutometry. Moreover, they demonstrated that this method was relatively safe with minimal side effects, the most prominent of which were pain, discomfort, and a feeling of crackling under the skin.

Ahmed and Mostafa conducted a study to compare the efficacy of carboxytherapy, platelet-rich plasma, and tripolar radiofrequency in the treatment of striae distensae ⁹. Their results elicited that all three modalities were equally efficient and safe; however, carboxytherapy and radiofrequency resulted in better patient satisfaction. Interestingly, Pinheiro *et al.* indicated that radiofrequency can

stimulate collagen synthesis at a better level compared to carboxytherapy¹⁰. Although they showed that carboxytherapy was more effective on striae rubra than alba, this was not statistically significant. Similarly, our results also showed no significant association between the type of striae and treatment outcome. Furthermore, in the mentioned study, platelet-rich plasma caused slightly more side effects than the other two modalities. This was in contrast to the Hodeib *et al.* study, which compared the efficacy of carboxytherapy with platelet-rich plasma in the treatment of striae¹¹. They reported that although both methods demonstrated significant improvement in striae alba, they were not significantly different in terms of efficacy, patient satisfaction, and side effects. However, histopathological examination revealed that carboxytherapy was superior in increasing the fibronectin expression compared with platelet-rich plasma. In contrast to the aforementioned studies, our results did not yield a significant effect for carboxytherapy on the treatment of striae. Nonetheless, some effects were observed. From 15 patients, three patients showed a good response, one patient showed a fair response, four patients showed a poor response, and 7 patients showed no response three months after 10 sessions of carboxytherapy across one-week intervals.

Also, most of our patients were females, which is compatible with other studies¹¹. The probable reason for this is that females usually seek medical attention for their striae due to the associated aesthetic burden. Furthermore, pregnancy is one of the main causes of striae formation and, as shown, was the second cause of striae in our study. Hence, women were expected to constitute a higher proportion of patients.

The main limitation of our study was the small sample size, which may have hampered our results in showing a significant effect of carboxytherapy. We did not include a control group to further assess the difference between other proposed modalities; instead, we used a before-after evaluation for each patient to decrease intergroup bias. Also, we tried to minimize bias by asking two dermatologists who were not involved in the study to evaluate the outcome of treatment. Moreover, we followed our patients for three months after the treatment was completed to assess the long-term effects of carboxytherapy. We recommend further research

that includes a control group and a larger sample size.

CONCLUSION

Striae are difficult to treat and patients are primarily concerned about the aesthetic outcome. Various modalities are available for its treatment but a search for a superior and more effective modality continues. Carboxytherapy has shown promising results in the treatment of striae and our study also demonstrated that this method is capable of correcting the striae in some cases; however, further studies with bigger sample sizes are required to ensure the efficacy of this modality in the treatment of striae.

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