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# Treatment of periorbital dark circles: Comparative study of carboxy therapy vs chemical peeling vs mesotherapy

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## Summary

**Objective:** Evaluation and comparison of the efficacy and safety of 3 different modalities of treatment for dark circles that function via different modes of action.

**Methods:** In total, 45 female patients with periorbital hyperpigmentation were randomly selected to participate from those attending the outpatient dermatology clinic of Al-Zahraa University Hospital within a 6-month period. Patients were divided into 3 groups, and the groups were subjected to different types of therapy: group A, carboxy therapy; group B, chemical peel; and group C, vitamin C mesotherapy.

**Results:** No statistically significant differences were detected in improvements in pigmentation or the degree of patient satisfaction between any of the groups. However, the mesotherapy group reported more of a burning sensation following treatment than the other 2 groups but also showed a significant improvement in pigmentation and patient satisfaction compared with the carboxy group.

**Conclusion:** All 3 treatment modalities were effective in the reduction in periorbital pigmentation. However, mesotherapy showed a significant improvement in pigmentation and a higher level of patient satisfaction compared with the other types of treatment.

## KEYWORDS

chemical peel, dark circles, mesotherapy, periorbital hyperpigmentation, vitamin C

## 1 | INTRODUCTION

Periorbital hyperpigmentation (POH) is an ill-defined condition that presents as a bilateral, round, homogenous, light-to-dark-colored brownish-black pigmentation surrounding the eyelids. It results in the appearance of tiredness in the patient.<sup>1</sup> This condition may be due to excessive pigmentation, thin and translucent lower eyelids, and shadowing owing to skin laxity and tear trough.<sup>2-4</sup> POH is challenging to treat and lacks a straightforward and reliable therapeutic strategy due to its complex pathogenesis and etiology.<sup>1</sup>

The objective of this study was to provide clinicians with a guide to the evaluation and treatment of POH using three therapeutic modalities. First, carboxy therapy is a noninvasive procedure that involves the transcutaneous injection of CO<sub>2</sub>. This procedure stimulates the production of new blood vessels by increasing the levels of growth factors. This increased blood flow supplies oxygen and

nutrients to the skin and vessels, which ultimately improves the appearance of the skin.<sup>5</sup>

Second, chemical peel therapy involves the application of lactic acid (LA, 15%) in combination with trichloroacetic acid (TCA, 3.75%) to the skin, and this has been used previously to treat POH by Vavouli et al<sup>6</sup> These chemicals cause controlled damage to the skin, following which regeneration and rejuvenation of the tissues occur during the healing process.<sup>7-9</sup>

Third, mesotherapy refers to a variety of minimally invasive techniques that consist of intracutaneous or subcutaneous liquid injections. Some of the more common chemicals that are injected in mesotherapy are vitamins such as vitamin C that can aid in facial skin repair.<sup>10,11</sup>

Vitamin C reduces POH as it inhibits the enzyme tyrosinase and has an antioxidant effect, thus preventing the production of free radicals that can trigger melanogenesis. It also promotes collagen

synthesis, which reduces dermal damage and leads to keratinocyte differentiation.<sup>11</sup>

## 2 | PATIENTS AND METHODS

In total, 45 female patients with POH were selected from those attending the outpatient dermatology clinic of Al-Zahraa University Hospital at Al-Azhar University in Cairo over a 6-month period from May 2015 to November 2015 to participate in this study. This study compared the effectiveness of three modalities of treatment: first, carbon dioxide therapy (carboxy therapy), second, chemical peel therapy using a combination of 2 peeling agents (TCA 3.75% and LA 15%), and third, vitamin C injection (vitamin C mesotherapy). After explaining each modality of treatment and the possible side effects, all patients were advised to avoid exposure of sunlight and general measures of sun protection as sunscreen and sunglasses were counseled at baseline of treatment and written confirmed consent was obtained from the patients who wished to participate in this study. Patients with a vascular type of periorbital pigmentation, or systemic disease-causing pigmentation, pregnancy, anemia, liver disease, or periorbital eczema, or those who had received laser treatment within the previous 12 months, were excluded from the study. Careful analysis of the medical history and a thorough general examination for clinical manifestations suggestive of any systemic disease or the presence of pigmentation in another area of the body or any other dermatological disease were performed. Dermatological examination of the periorbital area was also carried out to determine the type of dark circles (vascular type and tear trough were excluded by a stretch test).

The degree of darkness of pigmentation was classified as follows: Grade 1: light brown pigmentation, Grade 2: dark brown pigmentation, and Grade 3: black pigmentation.<sup>12</sup> The skin type was also determined according to the Fitzpatrick skin type classification. Patients were photographed using a digital camera (8 megapixels) before the start of treatment, and a blood sample was taken to test for complete blood count and liver function (SGOT, SGPT, alkaline

phosphatase, serum bilirubin, serum creatinine), before dividing patients into three groups randomly.

Group A (carboxy therapy group): 15 female patients underwent intradermal and subcutaneous injection of CO<sub>2</sub> at specific sites (Figure 1) on both the upper and lower eyelid bilaterally once a week for 5 weeks. The instrument used was the Rioblush™ for carboxy therapy, employing an A32 G needle with an infusion velocity of 50 mL/min. In total, 3 mL of gas was administered on each side, with an average time for each session of 5-8 minutes.

After treatment, the patients were advised to avoid external compression and report the presence of pain, edema, headache, or any other complications.

Group B (chemical peel group): 15 female patients were treated with chemical peel agents (TCA at 3.75% and LA at 15%) once a week for 5 weeks. The peel was a gel formulation. Patients were asked to close their eyes, and a degreasing wipe moistened with alcohol was used to remove any impurities and excess oil from the surface of the eyelid. Four layers of peel were applied to each peri-orbital area; the first layer of peel was applied in the area of intense pigmentation, and then the surrounding areas were treated. The duration of the first, second, and third layers of peel was 1-2 min, and the fourth layer was applied for about 5 minutes. The total time for a session ranged from 9 to 12 minutes. Then, the peel was neutralized with a wipe moistened with a 12% solution of arginine, and the patient washed the treated area with water. The patient was advised to avoid exposure to sunlight for 24 hours, but if exposed to direct light, she was recommended to use sunscreen and sunglasses. The color of the pigmentation following treatment was assessed according to an improvement score (from 0 to 4).<sup>13</sup> The level of patient satisfaction was also assessed.

Group C (mesotherapy group): 15 female patients were treated with mesotherapy, which included administration of an insulin syringe (30G LUER 0.30 × 4 mm needle). Vitamin C was extracted from an ampule (comprising the ingredients: ascorbic acid, aqua/water, disodium EDTA) using a large bore needle. About 10 mL was injected intraepidermally into both lower eyelids (5 mL for each eye) (Figure 2). Fine massage was performed after injection to decrease



**FIGURE 1** Injection sites for carboxy therapy group

the production of nodules. Ice cubes were also applied to reduce numbness and edema. Treatment was repeated 5 times at 1-week intervals.

**Evaluation of the treatment:** Evaluation of the treatment modalities was performed in all groups by assessing the level of patient satisfaction and the degree of improvement as determined by the investigator. The clinical response to treatment was assessed for each patient by comparing digital photographs taken before (baseline) and after treatment in the three groups.

Clinical assessment of the improvement in dark circles by the investigator was scored according to the following scale from 0 to iv<sup>13</sup>:

- (0) indicates no change in color
- (1) indicates mild improvement in color (<25%)
- (2) indicates moderate improvement in color (25%-50%)
- (3) indicates very good improvement in color (51%-75%)
- (4) indicates excellent improvement in color (>75% or normal skin color)

Upon final examination, patients were asked to score their level of overall satisfaction on a quartile scale: 0, not satisfied at all; 1, slightly satisfied; 2, moderately satisfied; and 3, highly satisfied.

## 2.1 | Statistical analysis (material and methods)

We calculate sample size according to Raosoft, and all statistical calculations were done using SPSS (statistical package for the social science version 25.00) statistical program at 0.05, 0.01, and 0.001 level of probability.<sup>14</sup> Quantitative data with nonparametric distribution were done using analysis of variance Kruskal-Wallis test, qualitative (categorical) data were presented by frequency, and percentage was calculated using Chi-square. The confidence interval was set to 95%, and the margin of error accepted was set to 5%. The *P* value was considered nonsignificant (NS) at the level of >.05, significant at the level of <.05 and .01, and highly significant at the level of <.001. Pearson linear correlation coefficient (*r*) was estimated to show the relationship between parameters.<sup>15</sup>

## 3 | RESULTS

In our study on 45 female patients with dark circles around their eyes, we found that median age of group A was 27 years, 27 years in group B, and 33 years in group C. The median of the duration of the dark circles before presentation is 5 years for group A, 5 years in group B, and 5 years in group C. Both groups A and C had positive family history of dark circles in 73.3%, while in group B, it was 40%.

Fitzpatrick type III was the most common skin type among the three groups, accounting for 40% of cases in group A, 60% of cases in group B, and 66.67% of cases in group C. In group A, a history of sleep deprivation was reported in 53.3% of cases, compared with 66.7% and 46.7% in groups B and C, respectively. In group A, 46.7% of cases reported a history of sun exposure compared with 53.3% and 40% in groups B and C, respectively. In group A, the percentage of patients that consumed excess levels of coffee was 20% compared with 33.3% and 26.7% in groups B and C, respectively. The most common pigmentation grade in group A was grade II in 53.3% of cases, whereas in groups B and C grade III pigmentation was observed in 53.3% of cases. There was no statistically significant difference between the three groups regarding the demographic data ( $P > .05$ ). Table 1 presents the descriptive statistics and the results of comparisons of the demographic data collected for the different groups.

Table 2 presents the degree of improvement in the dark circles and the level of patient satisfaction following therapeutic intervention for the three study groups. There was no statistically significant difference between the groups regarding the parentage of patients with different degrees of improvement after treatment ( $P > .05$ ), with 13.3% of group A showing excellent improvement (Figure 3A,B) compared with 26.7% of group B (Figure 4A,B) and 40% of group C (Figures 5A,B).

There was no statistically significant difference when comparing groups A, B, and C regarding patient's satisfaction after treatment ( $P > .05$ ). In total, 33.3% of group C patients described their satisfaction level as being excellent, compared with 0% and 6.7% in groups A and B, respectively. These data regarding satisfaction levels are presented in Table 2.



**FIGURE 2** Injection sites for vitamin C mesotherapy group

**TABLE 1** Descriptive statistics and results of comparison for demographic data collected on the studied groups

Demographic data		Groups						Kruskal-Wallis	P value
		Group A		Group B		Group C			
Age (years)	Range	18-51		14-55		22-48		1.096	0.578 ns
	Median	27		27		33			
Duration (years)	Range	1-15		1-23		1-15		4.596	0.100 ns
	Median	5		5		5			
		N	%	N	%	N	%	Chi-square	P value
Family history	Positive	11	73.3	6	40	11	73.3	4.727	.094 ns
	Negative	4	26.7	9	60	4	26.7		
Skin type	II	3	20	1	6.7	2	13.3	4.240	.644 ns
	III	6	40	9	60	10	66.7		
	IV	4	26.7	3	20	3	20		
	V	2	13.3	2	13.3	0	0		
Lack of sleep	Yes	8	53.3	10	66.7	7	46.7	1.260	.533 ns
	No	7	46.7	5	33.33	8	53.3		
Sun exposure	Yes	7	46.7	8	53.3	6	40	0.536	.765 ns
	No	8	53.3	7	46.7	9	60		
Smoking	Yes	11	73.3	10	66.7	11	73.3	0.216	.897 ns
	No	4	26.7	5	33.3	4	26.7		
Excess coffee	Yes	3	20	5	33.3	4	26.7	0.682	.711 ns
	No	12	80	10	66.7	11	73.3		
Pigmentation grade	I	2	13.3	2	13.3	1	6.7	1.994	.737 ns
	II	8	53.3	5	33.3	6	40		
	III	5	33.3	8	53.3	8	53.3		

ns, nonsignificant at  $P > .05$ .

**TABLE 2** Analysis and results of comparison of range of overall improvement and patient satisfaction results after intervention on the studied groups

Improvement data		Groups						Chi-square	P value
		Group A		Group B		Group C			
		N	%	N	%	N	%		
Overall improvement	No improvement	3	20	2	13.3	1	6.7	5.929	.431 ns
	Mild	8	53.3	4	26.7	5	33.3		
	Moderate	2	13.3	5	33.3	3	20		
	Excellent	2	13.3	4	26.7	6	40		
Patient satisfaction	Unsatisfied	3	20	2	13.3	1	6.7	10.200	.116 ns
	Mildly satisfied	8	53.3	5	33.3	5	33.3		
	Moderately satisfied	4	26.7	7	46.7	4	26.7		
	Excellent satisfied	0	0	1	6.7	5	33.3		

ns, nonsignificant at  $P > .05$ .

Pearson correlation analysis was performed between the degree of improvement and Fitzpatrick skin type, the grade of pigmentation, the duration of pigmentation, and patient satisfaction, and statistical significance was only detected between the degree of improvement and patient satisfaction ( $P = .000$ ,  $r = +.806$ ), as shown in Table 3.

Regarding treatment complications, there was no statistically significant difference between groups A, B, and C ( $P > .05$ ), although patients of group A complained more frequently of pain and edema of the eyelid (26.7%) as well as hematoma (20%), while patients in group C complaining more frequently of a burning sensation (26.7%). The data regarding treatment complications are presented in Table 4.

**FIGURE 3** Clinical photographs from group A. (A) Baseline and (B) clinically improved after 5 wk with patients' satisfaction and investigator score



**FIGURE 4** Clinical photographs from group B. (A) Baseline and (B) clinically improved after 5 wk with patients' satisfaction and investigator score



**FIGURE 5** Clinical photographs from group C. (A) Baseline and (B) clinically improved after 5 wk with patients' satisfaction and investigator score



**TABLE 3** Pearson correlation between the improvement and Fitzpatrick skin type, grade of pigmentation, duration of pigmentation, and patient satisfaction

	Patient satisfaction*	Fitzpatrick skin type	Grade of pigmentation	Duration of pigmentation
Improvement				
<i>P</i> value	.000	.057	.196	.362
<i>r</i>	+.806	-.286	+.197	+.139

\*Significant at  $P \leq .05$ .

## 4 | DISCUSSION

The development of dark circles under the eyes at any age is of great aesthetic concern because it may depict the individual as sad, tired, stressed, or old.<sup>9</sup> The periorbital area is one of the first facial regions to show the signs of aging. Even minor changes in its volume or structure can distort the perceived emotions and health of patients, possibly diminishing their confidence and well-being.<sup>16</sup>

The etiology of POH is multifactorial. It may be indicative of an underlying systemic disease (eg, Addison disease), an allergic reaction, nutritional deficiency, excessive sun exposure, or sleep disturbance. There is also most likely a familial component as this condition is often seen in family members over generations.<sup>17</sup>

Because of the complexity of its pathogenesis, various treatments are available for POH. In this study, we therefore compared the effectiveness of 3 modalities of treatment that operate via

different modes of action: carboxy therapy, chemical peel therapy with 15% lactic acid and mesotherapy with vitamin C.

These 3 modalities of treatment were tested in a controlled randomized study of 45 patients with dark circles around their eyes characterized mainly as Fitzpatrick type III. We found that there was no statistically significant difference between the three groups regarding the demographic data, or the parentage of patients with different degrees of improvement after treatment. These data confirmed that the three modalities of treatment were equally effective with no serious or permanent side effects reported in any of the groups. Our results were comparable with those of Hassan et al<sup>18</sup> who compared the efficacy of carboxy therapy and chemical peel therapy using TCA with the same concentrations and techniques used in our study. They found that with chemical peel therapy the degree of improvement was excellent in 46.7% of cases, good in 46.7% of cases and fair in 6.6% of cases, compared with carboxy treatment for which the degree of improvement was excellent in 46.7% of cases, good in 40% of cases and fair in 13.3% of cases, with no statistical difference between these 2 groups. These 2 methods of treatment were effective with minimal transient side effects. However, chemical peel therapy was cheap and easy to perform and therefore preferable for the treatment of POH compared with carboxy therapy that was expensive to perform.

In the current study, when comparing the results from each treatment modality, we found that the degree of improvement in POH patients in groups A and B was consistent with the findings

**TABLE 4** Analysis and results for comparison of complication after intervention on the studied groups

Improvement data		Groups						Chi-square	P value
		Group A		Group B		Group C			
		N	%	N	%	N	%		
Pain and edema of eyelid	Yes	4	26.7	1	6.7	1	6.7	3.462	.177 ns
	No	11	73.3	14	93.3	14	93.3		
Hematoma	Yes	3	20	0	0	1	6.7	3.841	.146 ns
	No	12	80	15	100	14	93.3		
Burning sensation	Yes	0	0	3	20	4	26.7	4.398	.111 ns
	No	15	100	12	80	11	73.3		

ns, nonsignificant at  $P > .05$ .

of a previous study by Vavouli et al<sup>6</sup>. Our data showed an improvement in pigmentation in all 3 groups, with no significant difference between groups A, B, and C, but group C showed a higher degree of excellent improvement compared with groups A and B.

Regarding patient satisfaction, Hassan et al<sup>18</sup> reported that carboxy therapy resulted in 40% very satisfied patients, 53% satisfied, and 6.7% slightly satisfied patients compared with the chemical peel group that resulted in 33.3% very satisfied patients, 53.3% satisfied, and 13.3% slightly satisfied patients, with no statistically significant differences. These results were in agreement with those reported by Vavouli et al<sup>6</sup>. In our study, we found that there was no statistically significant difference between groups A, B, and C regarding patient satisfaction after treatment ( $P > .05$ ). However, group C showed a higher degree of excellent satisfaction after treatment.

Regarding treatment complications, Hassan et al<sup>18</sup> and Vavouli et al<sup>6</sup> reported minimal side effects with chemical peel therapy with 20% of patients experiencing itching, 46.6% with a mild burning sensation, 33.3% with erythema exfoliation and 20% with dryness. In our study, most patients in the carboxy group tolerated minor pain at the site of injection and edema in 26.6% of cases, which usually disappeared within 10 minutes, but no patients reported a burning sensation, and the side effects were therefore not considered a restrictive factor. We conclude from our study that there was no statistical significant difference between groups A, B, and C. Patients of group C (26.7%) complained more frequently of a burning sensation, and although this was temporary, it did prevent two of the patients from completing their course of treatment (with one patient completing 3 sessions and the other patient only completing 2 sessions); all patients in the other groups completed their course of treatment. These results were in accordance with those of Paolo et al<sup>16</sup> and Hassan et al<sup>18</sup> who reported that for carboxy therapy and chemical peeling the compliance of patients was good and they tolerated the procedure well.

Patients in group A complained more frequently of pain and edema of the eyelid posttreatment (26.7%) as well as hematoma (20%), whereas patients in groups B and C complained of a burning sensation 20% and 26.7%, respectively. However, there was no

significant difference between groups A, B, and C regarding treatment complications, which was consistent with the findings of Hassan et al<sup>18</sup> and Vavouli et al<sup>6</sup>.

## 5 | CONCLUSION

All 3 treatment modalities tested were found to be effective in the reduction in periorbital pigmentation. However, mesotherapy was found to lead to the most significant improvement in pigmentation and the highest level of patient satisfaction, but the side effect of a burning sensation made it less tolerable in some patients.

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## REFERENCES

- Sarkar R, Ranjan R, Garg S, Garg VK, Sonthalia S, Bansal S. Periorbital hyperpigmentation: a comprehensive review. *J Clin Aesthet Dermatol*. 2016;9:49-55.
- Watabane S, Nakai K, Ohnishi T. Condition known as Dark Rings under the eyes in the Japanese population is a kind of dermal melanocytosis which can be successfully treated by Q - switched ruby laser. *Dermatol Surg*. 2006;32:785-789.
- Sheth PB, Shah HA, Dave JN. Periorbital Hyperpigmentation: a Study of its prevalence, common causative factors and its association with personal habits and other disorders. *Indian J Dermatol*. 2014;59: 151-157.
- Aghaei S. An approach to dark circles under the eyes. *J Surg Dermatol*. 2016;1:55-56.
- Zenker S. Carboxytherapy carbon dioxide injections in aesthetic medicine. *Prime-Journal*. 2012;2:1-12.
- Vavouli C, Katsambas A, Gregoriou S, et al. Chemical peeling with trichloroacetic acid and lactic acid for infraorbital dark circles. *J Cosmet Dermatol*. 2013;12:204-209.
- Khunger N. Standard guidelines of care for chemical peels. *Indian J Dermatol Venereol Leprol*. 2008;74:5-12.
- Roh MR, Chung KY. Infraorbital dark circles: definition, causes and treatment options. *Dermatol Surg*. 2009;35:1163-1171.

9. Vreck I, Ozgur O, Nakrat T. Infraorbital dark circles: a review of the pathogenesis, evaluation, and treatment. *J Cutan Aesthet Surg*. 2016;9:65-67.
10. Telang PS. Vitamin C in dermatology. *Indian Dermatol Online J*. 2013;4:1432.
11. Dayal S, Sahu P, Jain VK, Khatri S. Clinical efficacy and safety of 20% glycolic peel, 15% lactic peel, and topical 20% vitamin C in the constitutional type of periorbital melanosis: a comparative study. *J Cosmet Dermatol*. 2016;15:367-373.
12. El-Safouri OS, Abd El Fatah DS, Ibrahim M. Treatment of periorbital hyperpigmentation due to a lead of KOHL (surma) by penicillamine: a single group non-randomized clinical trial. *Indian J Dermatol*. 2009;54:361-363.
13. Oh DS, Kim DH, Roh TS, Yun IS, Kim YS. Correction of dark coloration of the lower eye lid skin with nano fat grafting. *Arch Aesthet Plast Surg*. 2014;20:92-96.
14. Snedecor GM, Cochran WG. *Statistical Methods*, 7th ed. Ames, IA: Iowa State University Press; 1982:325-330.
15. Härdle W, Simar L. *Applied Multivariate Statistical Analysis*, 2nd ed. Berlin: Springer; 2007:420 pp.
16. Paolo F, Nefer F, Paolo P, Nicolò S. Periorbital area rejuvenation using carbon dioxide therapy. *J Cosmetic Dermatol*. 2012;11:223-228.
17. Roberts WE. Periorbital hyperpigmentation: review of Etiology. *Med Evaluat Aesthet Treat*. 2014;13:472-482.
18. Hassan AM, Hassan GF, Aldalies HY, Elmaghraby GM. Treatment of periorbital dark circles: comparative study of chemical peeling with a combination of trichloroacetic acid and lactic acid versus carboxy therapy. *J Surg Dermatol* 2016;1:108-115.

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