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Review Article

Is there a gold standard for treating periorbital hyperpigmentation? – A narrative review of the latest evidence

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ABSTRACT

Background: Periorbital hyperpigmentation (POH) is a common esthetic concern, characterized by light to dark brown pigmentation or violaceous discoloration of the eyelids. It is multifactorial, associated with signs of aging and tiredness, and affects approximately 30% of individuals, predominantly women aged 16–25.

Objective: This narrative review aims to evaluate the efficacy of various treatments for POH, identifying potential gold standard therapies based on the latest evidence from clinical trials.

Methods: A comprehensive search was conducted on MEDLINE (PubMed) for clinical trials addressing POH treatments, excluding those focused on cosmetic interventions or the tear through type of POH. The initial search yielded 654 publications, with 18 studies meeting the inclusion criteria, encompassing a total of 619 participants.

Results: The reviewed studies evaluated a range of treatments, including platelet-rich plasma (PRP), laser therapy, carboxytherapy, chemical peels, microneedle fractional radiofrequency, and autologous fat. PRP showed high patient satisfaction but was less effective compared to chemical peels and emulsified fat in some studies. Laser therapies, particularly Q-switched Nd and carbon dioxide (CO_2) lasers, demonstrated favorable outcomes, with CO_2 laser showing higher efficacy and patient satisfaction than carboxytherapy and microneedling. Carboxytherapy was effective and well-tolerated but less potent than laser treatments. Chemical peels, especially those involving glycolic acid, showed rapid and significant improvement in pigmentation. Microneedle fractional radiofrequency and Vitamin C mesotherapy also proved beneficial, with the latter achieving the highest patient satisfaction despite procedural discomfort.

Conclusion: No single treatment modality emerged as a definitive gold standard for POH. Most treatments demonstrated effectiveness in reducing hyperpigmentation but fell short of complete eradication. The choice of treatment should be individualized, considering patient-specific factors and preferences. Further comparative studies are needed to optimize treatment strategies for POH.

Keywords: Periorbital hyperpigmentation, Dark circles, Periorbital darkening, Infraorbital hyperpigmentation

INTRODUCTION

Periorbital hyperpigmentation (POH) is a very common complaint in esthetic medicine appointments. It is described as a light to dark brown pigmentation or violaceous discoloration involving the upper and/or lower eyelids and causes significant concern among patients, as it is often associated with tiredness and signs of aging.[1]

Data on POH are limited due to its perception as a physiological phenomenon and its transient nature.[2] However, studies have shown that it is more prevalent among individuals aged 16–25 and predominantly affects women. It has an estimated prevalence of around 30%.[3]

Its etiology is typically multifactorial, with causes including loss of volume or skin laxity, excessive pigmentation, periorbital edema, and hypervascularity.[4] A recent study proposed a classification system for POH, dividing it into four types: Pigmentary, vascular, combination (pigmentary and vascular), and tear through, with the vascular type being the most common.[5]

Identifying the main cause of hyperpigmentation is crucial for determining the most appropriate treatment. This can be achieved through a combination of clinical examination and, depending on the author, evaluation with Wood's lamp and ultrasonography.[4]

Despite numerous treatments described for POH, it is still considered a resistant and challenging condition to treat. This study aims to conduct a systematic review of all available treatments for this condition.

MATERIAL AND METHODS

The search for eligible articles was conducted on MEDLINE (PubMed) using the combination of the terms (dark circles OR POH OR periocular hyperpigmentation OR periorbital darkening OR infraorbital darkening OR infraorbital dark circles). Only clinical trial studies written in English were included in the study. No time restriction was applied.

The study selection was performed by two authors and the articles were screened by title and subsequently by abstract. Exclusion criteria were (1) studies not classified as clinical trials, (2) studies conducted on non-human models, (3) investigations primarily centered on cosmetic interventions, and (4) research focusing on hollowing or tear through type of POH.

RESULTS

Our initial search identified 654 publications, which were reduced to a total of 55 studies, after selecting only clinical trials. Of those and after assessing the title, and when in doubt, the abstract, only 18 studies fulfilled the criteria with an aggregate of 619 participants.[6-23]

The articles are highly diverse, providing a comprehensive evaluation of most of the available treatments for POH [Table 1].

Among the 18 studies, five focus on using platelet-rich plasma (PRP) for the treatment of POH. One study examines PRP as a monotherapy, while others compare it with carboxytherapy, fat transfer, and chemical peelings.[7,9,11,12,16]

Regarding laser therapy, various types of treatments were assessed.[19] These included monotherapy with neodymium-doped yttrium aluminum garnet (Nd:YAG) laser, dual-wavelength picosecond Nd:YAG versus fractionated picosecond 755 nm alexandrite laser, and comparisons between Nd:YAG laser and carboxytherapy.[14,19,20] The carbon dioxide (CO_2) laser was compared with carboxytherapy in one study and with microneedling in another.[22,23] In addition, one study evaluated the use of Q-switched ruby laser (QSRL), and another examined the efficacy of Erbium-doped yttrium-aluminum-garnet (Er:YAG) laser with and without PRP injections.[13,21]

Carboxytherapy was evaluated not only in comparison with lasers, PRP, and in one study with peeling and mesotherapy but also as a monotherapy in three studies.[6,10,17,18]

In addition, one study assessed the efficacy of various types of chemical peelings for treating POH, while another investigated the role of microneedling.[8,15]

To evaluate the efficacy of existing treatments for POH, several studies were designed using only a single treatment modality.

Eyraud *et al.*, Roshdy *et al.,* and Seirafianpour *et al.* evaluated the effect of carboxytherapy on improving dark circles.[10,17,18] Eyraud *et al.* performed subcutaneous injection of CO_2 once a week for 3 weeks.[10] Using an infraorbital dark circle scale in pre and 6-month post-treatment photographs and three blinded evaluators, Eyraud *et al.* showed that carboxytherapy reduces skin discoloration and improves periorbital wrinkles without major side effects.[10] Seirafianpour *et al.* also performed subcutaneous injections of CO_2 only once a session every week for 4 weeks.[18] By assessing changes in periorbital pigmentation before, 1, and 5 weeks after the final session using Visioface and evaluating the patient satisfaction, the author showed a decrease in pigmentation post-intervention of around 20%, with patient satisfaction being higher, with 40% of the patients reporting good-to-excellent responses. Roshdy *et al.* aimed to study if different flow rates changed the therapeutic outcome of carboxytherapy by treating one group of patients with a flow rate of 30 ml/min and the other group with a flow rate of 60 mL/min, both weekly for 6 weeks.[17] Using melanin and erythema index, dark circle and hollowness grade, investigator global assessment, and patient satisfaction scale, Roshdy *et al.* showed that both flow rates were effective in the treatment of infraorbital dark circles. However, no difference was noted between both flow rates, with the higher rates causing more adverse effects.[17]

Continuing with the monotherapy studies, Mehryan *et al.* studied the effectiveness of PRP in the treatment of dark circles.[12] Using subjective (investigator and participant evaluation) and objective (with instrumental devices such as skin surface analyzer, Mexameter, and corneometer) evaluations, the author concluded that PRP can improve

infraorbital homogeneity but has no role in melanin content, stratum corneum hydration, periorbital wrinkles volume, or visibility index. However, 90% of the patients considered the results good or excellent.

Nilforoushzadeh *et al.*[15] also used subjective (investigator and participant evaluation) and objective (colorimeter, Mexameter, cutometer, skin ultrasound, and Visioface) evaluations to assess the efficacy of three sessions, 2 months apart of microneedle fractional radiofrequency in the treatment of periorbital dark circles. The results showed improvement not only in the periorbital skin lightness and elasticity while decreasing the percent change in skin color but it also decreased melanin content, improved skin density and thickness, and decreased wrinkles in the periorbital area. The outcomes were confirmed by the physician and patient's assessment, with 60% of patients describing an excellent reply.

Xu *et al.*[21] published the first report on treating infraorbital dark circles using a low-fluence 1,064 nm Q-switched laser (spot size of 3.5 mm, fluence of 4.2 J/cm^2, and repetition of rate of 5 Hz). Patients underwent eight sessions separated by 3–4 day intervals.

The outcomes were evaluated using noninvasive instruments such as a spectrophotometer, reflectance confocal microscopy (RCM), and a blind evaluation by three investigators based on before and after photographs as well as patient satisfaction. The study showed a decrease in melanin and erythema index decrease in melanin deposition in the upper dermis and both the investigator and the patient evaluation agreed.

The same author also evaluated the efficacy of the treatment with QSRL, since this type of laser is more selective for melanin compared to the Q-switched Nd:YAG laser (1,064 nm). The patients were treated with eight sessions separated by 7 days, with a wavelength of 694 nm, pulse duration of 40 ns, spot size of 7.1 × 7.1 mm, fluence of 3.0–3.5 J/cm^2, number of fractional dots 14 × 14, the diameter of each dot was 300 μm, and the distance between adjacent dots was 200 μm. The outcomes were evaluated using mexameter, RCM, global assessment by three blind investigators, and patient satisfaction. The global improvement showed 93.33% of excellent or good improvement with the vast majority of the patients rating their results as excellent or good. The objective evaluations also confirmed the efficacy of the QSRL by showing a decrease in erythema and melanin index and a clearance of melanin deposition. Vanaman Wilson *et al.*[19] evaluated the efficacy of one session of the dual wavelength picosecond Nd:YAG laser (first pass with 1,064 nm at 1.3 J/cm^2 and 5 Hz, followed by a second pass of 532 nm at 0.16J/cm^2 at 5Hz) and three sessions of the picosecond 755 nm alexandrite laser (through a fractionated lens with a 6 mm spot size and 0.71 J/cm^2 fluence at 1–5 Hz in a single pass) and the blinded-investigator assessment showed significant improvement with the latter and no improvement with the first laser.

The remaining studies focused on comparing various treatments in an attempt to identify the most effective option for POH.

Two studies compared two of the most used therapies for the treatment of dark circles – carboxytherapy and PRP.[7,16] Asilian *et al.,* using a split-face model, randomly assigned treatment with carboxytherapy once a week for 6 weeks and intradermal injections of PRP every 2 weeks for three sessions.[7] The outcome was evaluated by automatic assessment of skin vascularity and pigmentation in digital camera analysis, dermatologist blind evaluation, and patient self-assessment. Both the automatic assessment and the dermatologist assessment showed no statistically significant improvement after any technique or between the two. However, the patient's self-assessment showed improvement with both techniques, but again, not between the two. In terms of side effects, PRP has more remarkable ones, such as ecchymosis and pain. Nofal *et al.* also compared the two therapies, with the left periorbital area being treated with intradermal PRP injection every 2 weeks for seven sessions and the right side with carboxytherapy every week, also for seven sessions.[16] The periorbital darkness improvement was evaluated pre- and post-treatment and the patient self-evaluated. In this study, there was a statistically significant improvement in both sides, without difference between them. Complaints of pain and ecchymosis on the PRP-treated side caused some patients to refuse to complete all sessions.

Ahmed *et al.* focused on comparing carboxytherapy, chemical peeling (with a combination of trichloroacetic acid [TCA] 3.75% and lactic acid [LA] 15%), and Vitamin C mesotherapy by splitting the 45 patients into three groups.[6] The patients were treated once a week for 5 weeks. The outcomes were evaluated by comparing the degree of dark circles before and after treatment with digital photographs and patient satisfaction. In all the groups was an improvement in periorbital pigmentation without a statistically significant difference between them. However, among all of the therapies, mesotherapy showed the most impressive improvement in pigmentation and a higher level of patient satisfaction [Table 2].

Ellabban *et al.* compared the efficacy of four sessions, 2 weeks apart, of chemical peelings and PRP.[9] The patients were randomly divided into two groups, one treated with a peeling agent consisting of TCA 3.75% and LA 15% and the other with autologous PRP injections. The dark circles' improvement was assessed by digital photographs taken every session and evaluated by two dermatologists and by the patients. In both treatments, there was a statistically significant improvement in periocular dark circles, with a

high statistically significant difference in favor of chemical peeling, which was confirmed by patient satisfaction.

Dayal *et al.* proposed to compare different types of peelings and Vitamin C.[8] For that, the author randomly distributed the patients into three groups, the first one being treated with 20% glycolic acid peel, the second group with 15% lactic peel, and the third group only applying 20% topical Vitamin C daily. The two dermatologist assessments of the percentage of pigmentary clearance showed that the clinical improvement was maximum and fastest with the glycolic peel group, followed by the lactic peel group. However, all three groups had some level of skin lightening.

Kadry *et al.* aimed to evaluate whether combined fat transfer and nanofat were more effective than PRP in treating infraorbital dark circles.[11] For that, 30 patients were randomized into two groups: One was treated with PRP injections every 4 weeks for 3 sessions, and the other was injected with fat and emulsified fat in one session. Both the clinical assessment and the patient satisfaction showed superiority in terms of improvement and satisfaction with autologous emulsified fat.

The next group of studies aims to compare different types of lasers with each other or with different types of POH treatments.

Zaheri *et al.* compared the effects of four bi-weekly sessions of carboxytherapy on one side of the face with fractional CO_2 laser therapy on the other.[22] Both physician and patient assessments indicated that CO_2 laser therapy resulted in greater improvement and higher patient satisfaction, with side effects similar to those of carboxytherapy.

Carboxytherapy was also compared with fractional Q-switched Nd:YAG laser in a study conducted by Nilforoushzade*h et al.*,[14] in which the patients were divided into two groups, with one group treated by six sessions of carboxytherapy and the other group treated with four sessions of 1,064 nm fractional Q-switched Nd:YAG laser (fluency of 1.3 J/cm^2, pulse rate of 5 Hz, spot size of 7 × 7 mm, energy 500 spot size, and a pulse duration of 5 ns).[14] The results were evaluated by objective assessment using a colorimeter, cutometer, Mexameter, and skin ultrasound imaging system and physician and patient satisfaction, and although both treatments showed to be effective in the treatment of POH, carboxytherapy proved to be significantly more effective by increasing skin lightness and decrease in melanin content.

In a study by Zamanian *et al.*, CO_2 laser therapy was compared with microneedling for treating dark circles.[23] One group received fractional CO_2 laser treatment (power: 15; stack: 1; pulse duration: 1000; and spacing: 1000), while the other was treated with microneedling combined with topical TCA 10% application. Objective assessments, based on the difference in darkness intensity in digital photographs, along with evaluations by physicians and patients, indicated higher efficacy and satisfaction for the CO_2 laser treatment.

Finally, Nilforoushzadeh *et al.*[13] evaluated whether combination therapy was superior to monotherapy by treating the right periorbital side with a combination of long pulse Er:YAG laser with energy of 500–700 mJ and autologous PRP, and the left side with only the Er:YAG laser.[13] Both treatments were administered in three sessions at 4-week intervals. The evaluation utilized objective instruments (colorimeter, cutometer, Visioface, and Mexameter), along with assessments by independent blinded investigators and patient satisfaction ratings. While both treatments proved effective, the combination therapy showed superior results across all evaluated parameters, including skin lightness, percent change in color, and reduction of wrinkles, as well as higher patient and physician satisfaction.

DISCUSSION

As we can see from the results above, there are a lot of different treatments available for POH, mostly due to its complexity and various etiologies. In this systematic review, we focused on the POH, excluding the tear-through type.

With this article, we aimed to evaluate the most common treatments for POH, focusing on clinical trials that provided evidence-based insights. The treatments assessed included PRP, laser therapy, carboxytherapy, chemical peels, microneedle fractional radiofrequency, and autologous fat, and one of the most prominent findings is that while most treatments are effective in reducing POH, none of them completely eradicated it.

PRP was evaluated in five studies and while in monotherapy it improved infraorbital homogeneity and the patient satisfaction was extremely high, when in comparison with other treatments (such as chemical peelings or emulsified fat), it appeared to be less effective.[7,9,11,12,16] When studied in combination with laser Er:YAG, it boosted the efficacy of the laser, contributing to superior results in skin lightness, percent change in color, and reduction of wrinkles as well as higher patient satisfaction.[13] Based on the reviewed studies, PRP is generally considered an effective treatment for POH, though it is likely not the most potent option when used alone. It appears to enhance efficacy when combined with other treatments.

Various types of lasers have been evaluated in studies, including Q-switched Nd:YAG laser, CO_2 laser, QSRL, and Er:YAG laser. In terms of monotherapy, both Q-switched Nd:YAG laser and QSRL demonstrated favorable outcomes in objective measurements and patient satisfaction.[20,21] However, when compared to carboxytherapy, the Nd:YAG laser, while effective for POH, showed reduced efficacy and increased side effects.[14] A study evaluating fractionated

Table 1: Characteristics of the studies included.

Author	Year	Study design	*n*	Inclusion/ exclusion criteria	Blinding
Ahmed *et al.*[6]	2018	Randomized controlled trial. One group underwent intradermal and subcutaneous injection of CO_2, the second group was treated with a chemical peel (TCA+LA) and the third group was treated with mesotherapy and Vitamin C. All the treatments were administered once a week for 5 weeks	45	Clearly defined	NR
Asilian *et al.*[7]	2021	Randomized clinical trial. The patients were treated with carboxytherapy (5 cc once a week for 6 weeks) on one randomly assigned side of the face and PRP (intradermal injections every 2 weeks for three sessions) on the other	21	Clearly defined	Yes
Dayal *et al.*[8]	2016	Randomized controlled trial. The first group and second group underwent 3-weekly peels, the first 20% GA peel and the latter 15% lactic peel. The third group applied 20% topical Vitamin C daily. The duration of the therapy was 12 weeks	90	Clearly defined	No
Ellabban *et al.*[9]	2019	Randomized controlled trial. One group of patients was treated with a chemical peeling (TCA 3.75%+LA 15%) and the other group received autologous PRP injections, both every 2 weeks for four sessions	42	Clearly defined	NR
Eyraud *et al.*[10]	2021	Clinical trial. Subcutaneous injection of CO_2 once a week for 3 weeks	35	Clearly defined	Yes
Kadry *et al.*[11]	2023	Randomized controlled trial. One group of patients was treated with PRP and another group with autologous fat transfer with emulsified fat injection	30	Clearly defined	Yes
Mehryan *et al.*[12]	2014	Clinical trial. The patients were treated with a single session of intradermal injections of PRP	10	Clearly defined	Yes
Nilforoushzadeh *et al.*[13]	2021	Clinical trial. The right periorbital side was treated with Er: YAG laser+PRP and the other side only with Er: YAG	32	Clearly defined	Yes
Nilforoushzadeh *et al.*[14]	2021	Randomized controlled trial. One group received six sessions carboxytherapy and the other group laser Nd: YAG Q-Switched for four sessions	28	Clearly defined	NR
Nilforoushzadeh *et al.*[15]	2023	Clinical trial. The patients were treated with microneedle fractional radiofrequency every 2 months, three sessions.	9	Clearly defined	NR
Nofal *et al.*[16]	2018	Clinical trial. In the left periorbital area, the patients were treated with intradermal PRP injection every 2 weeks and on the right side with carboxytherapy every week, both for seven sessions	30	Clearly defined	NR
Roshdy *et al.*[17]	2021	Randomized controlled trial. One group received carboxytherapy at a flow rate of 30 mL/min and the other at 60 mL/min weekly for 6 weeks	80	Clearly defined	NR
Seirafianpour *et al.*[18]	2024	Clinical trial. Patients underwent intradermal carboxytherapy (10–20 mL of CO_2 at a rate of 20 mL/min and a temperature of 15°C for a duration ranging from a few seconds to 1 min) once a week for 4 weeks	20	Clearly defined	Yes
Vanaman Wilson *et al.*[19]	2017	Controlled clinical trial. One group was treated with one single session of dual wavelength picosecond Nd: YAG laser (1,064/532 nm) and the other with picosecond 755 nm alexandrite laser in three sessions with 3 weeks intervals.	30	Clearly defined	Yes
Xu *et al.*[20]	2011	Clinical trial. The patients underwent eight sessions of low-fluence 1,064 nm Q-switched Nd: YAG laser treatment at 3–4 day intervals	30	Clearly defined	Yes
Xu *et al.*[21]	2016	Clinical trial. The patients were treated with eight sessions separated by 7 days of fractional Q-switched ruby laser	30	Clearly defined	Yes

(Contd...)

Table 1: *(Continued).*

Author	Year	Study design	*n*	Inclusion/ exclusion criteria	Blinding
Zaheri *et al.*[22]	2022	Randomized controlled trial. On one side of the periorbital area was administered carboxytherapy and the other side fractional CO_2 laser therapy in four sessions at 2-week interval	30	Clearly defined	NR
Zamanian *et al.*[23]	2019	Randomized controlled trial. One group of patients was treated with microneedling with TCA 10% cream topically and the other group with fractional CO_2 laser. Both groups had three sessions with 1 month interval	27	Clearly defined	NR

NR: Not reported, CO_2: Carbon dioxide, Nd: YAG: Neodymium-doped yttrium aluminium garnet, Er: YAG: Erbium-doped yttrium-aluminum-garnet, TCA: Trichloroacetic acid, LA: Lactic acid, PRP: Platelet-rich plasma

Table 2: Summary of the outcome and results of the studies included.

Author	Year	Outcome	Results
Ahmed *et al.*[6]	2018	Outcome was improvement in dark circles and level of patient satisfaction	All treatment modalities improve periorbital pigmentation with little side effects. Mesotherapy had the most significant improvement and level of patient satisfaction
Asilian *et al.*[7]	2021	Outcome was periorbital darkness evaluated by blinded dermatologist and patient self-assessment with the help of visual analogue scale and automatic assessments of skin vascularity and pigmentation in digital camera analysis. Secondary outcome was procedure-related side effects.	There was a slight improvement in POH before and after both approaches, but statistically insignificant. The patients' opinion revealed statistically relevant improvement in both techniques. The side effects were more remarkable in PRP
Dayal *et al.*[8]	2016	Outcome was the percentage of pigmentary clearance assessed by two dermatologists based on high-resolution photographs. Secondary outcomes included patients and physician global assessment	Pigmentary clearance was higher with glycolic peel, making it the most effective treatment, followed by lactic acid. It also had the best physician and patient global assessment
Ellabban *et al.*[9]	2019	The outcome was the degree of improvement of infraorbital hyperpigmentation assessed by two dermatologists using digital photographs and patient satisfaction.	Both PRP and chemical peeling are effective in improving POH, with the latter being more effective. The patient satisfaction agrees with the findings.
Eyraud *et al.*[10]	2021	Outcome was improvement of infraorbital dark circles assessed by three blinded doctors (plastic surgeon, maxillofacial surgeon, and dermatologist) and the patient themself. The secondary outcome was reduction of lower eyelid wrinkles, tolerance of pain during injection and complications	Carboxytherapy is effective in reducing infraorbital dark circles and wrinkles of the eyelid. No complications were described.
Kadry *et al.*[11]	2023	Primary outcome was defined as the improvement of the dark circles rated by two blinded dermatologists. Secondary outcomes included patient satisfaction and post-operative complications	Emulsified fat is much more effective than PRP in the treatment of dark circles. The patient's satisfaction corroborates the results.
Mehryan *et al.*[12]	2014	The outcome was evaluated by a blinded investigator with the help of skin surface analyzer, mexameter and a corneometer. Participants' satisfaction was assessed.	PRP showed improvement in infraorbital color homogeneity but no changes in melanin content, stratum corneum hydration, periorbital wrinkles volume or visibility index. 90% of patients thought the results were good/excellent.
Nilforoushzadeh *et al.*[13]	2021	Outcome was evaluated by biometer characteristics using a colorimeter, cutometer, Visioface and Mexameter. Physician assessment and patient satisfaction was also evaluated	The side treated with the combination of PRP+Er: YAG laser showed decreased melanin content, increase in skin lightness

(Contd...)

Table 2: *(Continued).*

Author		Outcome	Results
			and higher decrease in the percent change of the color and wrinkles. The patient satisfaction was also higher in combination treatment.
Nilforoushzadeh *et al.*[14]	2021	Outcome was evaluated using a colorimeter, cutometer, Mexameter, and skin ultrasound imaging system. Physician assessment and patient satisfaction was also evaluated	Carboxytherapy is more effective than Nd: YAG laser and has less side effects. The physician assessment corroborates the findings.
Nilforoushzadeh *et al.*[15]	2023	The outcomes were evaluated before and after the treatment by means of colorimeter, Mexameter, cutometer, skin ultrasound, and Visioface. Secondary outcome was patient satisfaction and physician assessment	The evaluation showed improvement in skin lightness, elasticity, and density, decrease in melanin content, skin color and wrinkles. Patient and physician assessment were also positive
Nofal *et al.*[16]	2018	Outcome was improvement in POH evaluated by investigators' assessment of photographs, visual analog scale, and patient satisfaction	Both treatments are effective without a significant difference between them. Patient satisfaction was similar in both but carboxytherapy is better tolerated than PRP
Roshdy *et al*[17]	2021	Evaluation was based on melanin and erythema index, dark circle grade, hollowness, investigator global assessment, and patient satisfaction scale. Outcome was improvement of the dark circles. Secondary outcomes included patient satisfaction and complications rate	Both flow rates are effective as a treatment of dark circles. No difference found in dark circle improvement, melanin/erythema index, infraorbital hollowness, investigator global assessment or patient's satisfaction between both flow groups.
Seirafianpour *et al.*[18]	2024	Primary outcome was defined as the variation in periorbital pigmentation (ΔE) before and after the trial, using Visioface. Secondary outcomes included patient satisfaction	A notable decrease in pigmentation was noted. Patient satisfaction exceeded ΔE changes
Vanaman Wilson *et al.*[19]	2017	Outcome was the degree of improvement of infraorbital hyperpigmentation. Patient satisfaction and side effects were also evaluated	A single treatment with dual wavelength picosecond Nd: YAG laser does not improve infraorbital hyperpigmentation. A series of treatments with the fractionated picosecond 755 nm alexandrite laser improved hyperpigmentation. Patient satisfaction was high in both trials.
Xu *et al.*[20]	2011	Evaluation was based on investigator assessment, patient satisfaction, mexameter, reflectance confocal microscopy and adverse effects.	Blind evaluation showed improvement after treatment, with a decrease in melanin and erythema index and melanin deposition in upper dermis. Patient satisfaction was good/ excellent and adverse effects were minimal.
Xu *et al.*[21]	2016	Clinical and instrumental outcomes were evaluated before, during and after the end of treatment by means of mexameter, reflectance confocal microscopy, investigator assessment and patient satisfaction	The treatment is safe and effective as assessed by blind evaluation, with a significantly decrease in melanin and erythema index and a decrease in melanin deposition
Zaheri *et al.*[22]	2022	Outcome was POH improvement assessed by the patient and the physician. Objective assessment was made by photo-documenting.	Fractional CO_2 laser appears to have superior results when compared to carboxytherapy
Zamanian *et al.*[23]	2019	Outcome was improvement of skin darkening in digital photographs, physician's judgment and patients' satisfaction	The improvement and patient satisfaction was significantly higher in the group treated with fractional CO_2 laser

CO_2: Carbon dioxide, Nd: YAG: Neodymium-doped yttrium aluminium garnet, Er: YAG: Erbium-doped yttrium-aluminum-garnet, PRP: Platelet-rich plasma, POH: Periorbital hyperpigmentation

picosecond lasers revealed that the 755 nm alexandrite laser improved hyperpigmentation, unlike the dual-wavelength picosecond Nd:YAG laser.[19] Conversely, CO_2 laser lacked direct studies on its efficacy in monotherapy but exhibited superior results and higher patient satisfaction compared to carboxytherapy and microneedling.[22,23] It's worth noting that only a single treatment was administered with the dual-wavelength picosecond Nd:YAG laser, whereas a series of treatments were performed with the 755 nm alexandrite laser. The ER: YAG laser also demonstrated effectiveness in treating dark circles and periorbital wrinkles, with enhancement of these results when combined with PRP.[13]

It is known that injection of CO_2 into tissue induces hypercapnia, increasing blood flow and thereby stimulating the production of growth factors that promote the formation of new blood vessels, collagen and elastin.[10] Carboxytherapy, investigated in three articles as monotherapy, consistently demonstrated efficacy in improving periorbital pigmentation, high patient satisfaction, ease of use, and high tolerability.[10,17,18] However, concerns persist regarding the mode of administration and the required number of sessions. Research suggests that three sessions are generally sufficient to achieve results while maintaining patient compliance, with higher flow rates not necessarily correlating with improved outcomes. Lower flow rates are preferred due to comparable efficacy with fewer side effects in treating dark circles. Comparative studies with PRP peels and mesotherapy found carboxytherapy to yield similar results in improving POH.[6,7,16] Nevertheless, when compared to lasers such as CO_2 and Q-switched 1,064 nm Nd:YAG, carboxytherapy showed inferior efficacy.[14,22] Despite this, the majority of the eight studies, including carboxytherapy, reported improvements in periorbital pigmentation and patient satisfaction, underscoring its continued relevance as a treatment option.

Peelings have been proposed as a treatment in the POH due to their capacity to eliminate melanin from the stratum corneum and epidermis.[24] In the study of Dayal *et al.,* the authors concluded that alpha hydroxy acids (20% glycolic peeling and 15% LA peeling) are effective, with the glycolic peeling being more effective and having the fastest results, despite being the one with the most side effects.[8] Ellabban *et al.* also confirmed the efficacy of the chemical peelings (in this study, TCA 3.75% + LA 15% was used) and showed its superiority in efficacy, tolerance, and patient satisfaction when in comparison with PRP.[9] Finally, Ahmed *et al.* compared the chemical peelings (TCA 3.75% + LA 15%) with carboxytherapy and Vitamin C mesotherapy, again corroborating the hypothesis that chemical peelings are an effective weapon in treating POH.[6]

Vitamin C mesotherapy merits mention as a valuable agent for treating dark circles. In the study by Ahmed *et al.* discussed above, while it did not demonstrate statistical superiority over other treatments, it resulted in the most significant improvement in pigmentation and the highest level of patient satisfaction.[6] The only drawback reported was a burning sensation experienced during the procedure.

In a study by Nilforoushzadeh *et al.,* microneedle fractional radiofrequency emerged as a viable option for treating hyperpigmentation.[15] It not only diminishes melanin and improves skin lightness, elasticity, density, and thickness in the periorbital area, but it also improves wrinkles.

CONCLUSION

POH remains a significant concern in esthetic medicine, often associated with tiredness and signs of aging. Despite its prevalence, limited data and the multifactorial etiology of this condition present substantial challenges in selecting effective treatments. A narrative review of clinical trials highlighted in this study assessed various treatment modalities for POH. Many treatments demonstrated partial but notable improvements, even if they did not fully eliminate the pigmentation.

The clinical trials reviewed involved a diverse range of interventions, each one with advantages and limitations, emphasizing the need for tailored approaches based on individual patient characteristics and preferences. For instance, PRP enhances skin homogeneity and is generally associated with good patient satisfaction. However, it carries a risk of notable side effects in certain cases, which may impact individual experiences. Carboxytherapy effectively reduces periorbital pigmentation, significant improvement in skin lightness and decreased melanin content while offering high patient satisfaction, ease of use, and excellent tolerability. Laser therapies, such as QSRL and fractional CO_2 laser, showed significant reductions in pigmentation and improved skin texture, though not all patients achieved the desired outcomes with every modality. Microneedling combined with topical treatments proved effective in enhancing skin elasticity and reducing pigmentation.

Furthermore, comparisons between different treatment strategies highlighted the potential benefits of combination therapies. For instance, combining long-pulse Er:YAG laser with PRP yielded superior results over monotherapy alone, offering enhanced skin lightness, reduced pigmentation, and higher patient satisfaction. These findings suggest that a one-size-fits-all approach may not be optimal for treating POH, as individual patient response varies widely based on factors such as skin type, the degree of pigmentation, and the presence of underlying conditions.

Given the limited data and the diverse treatment outcomes observed across the reviewed studies, further research and comparative studies are warranted to elucidate optimal treatment strategies for this challenging condition. Future studies should focus on long-term outcomes, patient-centered assessments, and the development of new, innovative approaches to managing POH effectively.

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