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Original Article

Platelet-Rich Plasma versus Platelet-Rich Fibrin in the Treatment of Periorbital Dark Circles: A Split Face Comparative Study

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ABSTRACT

Background: Periorbital hyperpigmentation (POH) as a common cosmetic concern has multifactorial etiology and limited effective therapies. Platelet-rich plasma (PRP) widely been used for skin rejuvenation, whereas platelet-rich fibrin (PRF), that is a second-generation platelet concentrate, offers an option for sustained growth factor release and superior outcomes. The study aim was to compare the efficacy, safety, as well as patient satisfaction of PRP compared to PRF injections in the treatment of POH.

Methods: A randomized controlled split-face study was performed on 37 patients with POH, the right infraorbital area received PRP and the left received PRF. Patients underwent three intradermal injection sessions at three-week intervals. Efficacy was evaluated at 10 weeks using clinical grading, therapeutic response, and patient satisfaction scales. Safety and tolerability were recorded, and patients were followed for 2 months.

Results: Both treatments produced significant improvement compared to baseline (p=0.0001). PRF demonstrated superior outcomes, with higher regression of lesion grade (64.9% improved to grade 1 and 10.8% achieved complete clearance vs 8.2% grade 1 improvement with PRP; χ^2=36.17, p=0.0001). Therapeutic response was significantly better with PRF (29.7% moderate, 16.2% good, 10.8% complete) compared to predominantly mild response with PRP (73.0%) (χ^2=44.96, p=0.0001). Patient satisfaction was markedly higher with PRF, with 62.2% very satisfied versus none on the PRP side (χ^2=38.4, p=0.0001). PRF response was significantly better in lower eyelid-only cases (p=0.021) and in moderate baseline grades compared to severe cases (p=0.0001).

Conclusion: Both PRP as well as PRF are safe treatment modalities and effective for POH management. However, PRF demonstrated significantly superior clinical improvement and higher patient satisfaction, particularly in patients with moderate severity and lower eyelid involvement. PRF may be considered a preferable therapeutic option for POH.

Keywords: Platelet-Rich Plasma, Platelet-Rich Fibrin, Periorbital Dark Circles.

INTRODUCTION

Dark circles are characterized by bilateral, round, homogeneous pigmented macules in the infraorbital region. Periorbital hyperpigmentation (POH) is a common cosmetic condition affecting

both young and elderly individuals, with hereditary factors being the predominant cause. This occurs more frequently in individuals with darker skin types [1]. It is often perceived as a sign of fatigue, but its etiology is multifactorial. Several factors have been implicated, including chronic sun exposure, allergies, dehydration, vitamin deficiencies, smoking, and local irritation. Anatomical factors also play a role, since the infraorbital region has minimal subcutaneous fat, which predisposes to venous stasis and edema. Additionally, the eyelid skin is very thin, making underlying vasculature more visible and contributing to a shadowing effect [2].

Differentiating true hyperpigmentation from shadowing caused by tear trough deformity is crucial for proper management. Based on clinical assessment, true POH has been classified into four subtypes: vascular (bluish or purplish discoloration often with edema), pigmented (brown discoloration), structural (shadows due to facial contour), and mixed, which combines these patterns [3].

Several non-surgical interventions are available for periorbital rejuvenation, including chemical peeling, microneedling, fractional lasers, carboxytherapy, and hyaluronic acid fillers, while surgical options include blepharoplasty, fat transfer, and facelifts. Recently, platelet-rich plasma (PRP) has gained popularity as a minimally invasive treatment for periorbital pigmentation [4]. Its beneficial effects are attributed to its bioactive molecules. Growth factors released upon platelet activation stimulate basement membrane repair through laminin and collagen IV, reduce melanin synthesis via epidermal growth factor (EGF) in addition to the transforming growth factor β (TGF-β), and promote dermal thickening by enhancing collagen production and hyaluronic acid synthesis under effects of platelet-derived growth factor (PDGF) [5].

The second-generation platelet concentrate, platelet-rich fibrin (PRF), was later developed as a simplified alternative to PRP. Unlike PRP, PRF does not require anticoagulants or thrombin during preparation. Its three-dimensional fibrin network functions as a natural scaffold capable of entrapping and gradually releasing multiple growth factors such as vascular endothelial growth factor (VEGF), TGF-β1, insulin-like growth factor (IGF), as well as PDGF. PRF also has the ability to recruit circulating stem cells, supporting angiogenesis and tissue regeneration [6]. Compared with PRP, it provides a more gradual and sustained release of bioactive molecules and avoids potential hypersensitivity reactions associated with anticoagulant use [7].

PRP and PRF are considered simple, cost-effective modalities for periorbital rejuvenation with short downtime and high patient satisfaction. Evidence suggests that the fibrin matrix of PRF enhances cell migration and proliferation, potentially offering superior therapeutic outcomes compared to PRP [7].

Although both PRP and PRF have been explored in dermatological applications, comparative studies specifically addressing their role in periorbital hyperpigmentation remain limited. Up to our knowledge, no similar studies have been carried out at Dermatology, Venerology and Andrology department, Faculty of Medicine, Zagazig University Hospitals. Therefore, this study aim was to compare the efficacy and safety of platelet-rich plasma vs platelet-rich fibrin in the management of periorbital hyperpigmentation.

METHODS

We performed this randomized controlled split-face clinical study on 37 adult patients with clinically diagnosed POH at the

Outpatient Clinic of the Dermatology, Venereology, and Andrology Department, Faculty of Medicine, Zagazig University Hospitals through 1 year from January 2024 to May 2025.

The sample size was evaluated utilizing a power analysis assuming a medium effect size, with 80% power and a 5% significance level, resulting in a minimum requirement of 30 participants. To compensate for potential dropouts, 37 patients were included. Randomization was performed using a computer-generated sequence, and allocation to treatment sides (PRP for the right side, PRF for the left side) was concealed by sealed opaque envelopes. [8]

The study protocol was reviewed and approved by the Institutional Review Board of Zagazig University (ZU-IRB# 9212-13-3-2022). Written informed consent was obtained from all participants prior to enrollment. All human research procedures were performed in accordance with the principles of the Declaration of Helsinki.

Thirty-seven patients with clinically diagnosed POH were recruited. Included patients were adults aged 20 to 51 years with dark circles confirmed by dermatological examination. Patients were excluded if they were pregnant or lactating, had dermatological diseases or scars in the periorbital region, or suffered from systemic illnesses such as diabetes mellitus, anemia, or chronic infections.

Clinical Assessment:

All participants underwent thorough history taking, including age, sex, occupation, lifestyle habits, family history, and previous treatments. General examination was carried out to exclude systemic diseases, and dermatological assessment was performed to classify POH according to the combined system of Ranu et al [9] and Huang et al [10], which categorizes POH into constitutional, vascular, post-inflammatory, and shadow-related types. The severity of pigmentation was graded according to the scale of Sheth et al [11], ranging from 0 (comparable to adjacent skin) to 4 (severe pigmentation spreading beyond the infraorbital folds). Standardized photographs were obtained before treatment and at follow-up visits.

Interventions:

The PRP was obtained by withdrawing 10 ml of venous blood into anticoagulant-containing tubes. The collected samples were subjected to centrifugation at 3500 rpm for 10 minutes, which allowed stratification into three distinct layers: red blood cells at the base, platelet-poor plasma at the top, and a middle layer enriched with platelets. From this, nearly 3 ml of PRP was harvested for subsequent injection [12]. For preparation of PRF, an equal volume of venous blood (10 ml) was drawn into plain tubes without the addition of anticoagulant. These tubes were immediately centrifuged at 800 rpm for 6 minutes, yielding an upper fraction of approximately 1 ml that represented the fluid PRF. This remained injectable for about 10 minutes before transforming into a fibrin gel, requiring immediate administration [13].

Both PRP and PRF were injected intradermally into the infraorbital region using a 25-gauge blunt cannula. Linear threading and depot techniques were used, and treatments were repeated every three weeks for a total of three sessions.

Outcome Assessment and Follow up:

The Efficacy of treatment was evaluated at the end of 10 weeks using two methods. First, clinical improvement was assessed by two independent blinded dermatologists who compared standardized pre- and post-treatment photographs according to the scale described by Mehryan et al [14], which grades improvement as none (0–25%), fair (26–50%), good (51–75%), or excellent (>75%). Second, patient satisfaction was measured using a 4-point scale (0–3)

ranging from "not satisfied" to "very satisfied" [14]. Safety and tolerability were assessed through documentation of local adverse effects including pain, bruising, edema, or infection. Patients were followed for an additional two months after completion of therapy to monitor for recurrence of pigmentation.

Statistical Analysis:

Statistical analysis was performed with SPSS v23.0 (IBM Corp., Armonk, NY, 2015). Data with normal distribution were shown as mean ± SD, whereas skewed data were given as median (range). Group differences were tested using ANOVA or Kruskal–Wallis as appropriate. Marginal homogeneity was applied for paired ordinal data, and Chi-square for categorical variables. A p-value <0.05 was considered significant.

RESULTS

The study population (n = 37) had a mean age of 33.1 ± 8.7 years (range: 20–51), with a female predominance (64.9%). Workers constituted 75.7% of participants, while housewives accounted for 24.3%. Median disease duration was 4 years (range: 0.25–15). Skin phototype III was most frequent (62.2%), followed by type II (27.0%), with types I and IV each representing 5.4%. All cases presented with hyperpigmentation; shade and vascular types were less common, recorded in 16.2% and 13.5% respectively. Lesions were localized to the lower eyelid in 70.3% and involved both eyelids in 29.7%. Family history was positive in 35.1% of cases. Among risk factors, stress (27.0%), insomnia (24.3%), refractive errors requiring glasses (21.6%), and prolonged TV watching (21.6%) were most reported, while cosmetic use (10.8%) and smoking (5.4%) were less frequent (Table 1).

Before treatment, lesion grades were identical on both sides, with the majority presenting as grade 3 (43.2%) and grade 4 (51.4%). After treatment, significant improvement was observed on both sides ($p1 = 0.0001$), with marked differences between PRP and PRF outcomes ($\chi^2 = 36.17$, $p = 0.0001$). On the PRP side, most patients remained in grade 2 (48.6%) or grade 3 (37.8%), with only 8.2% improving to grade 1. In contrast, the PRF side demonstrated substantial regression, with 64.9% improving to grade 1, 18.9% to grade 2, 10.8% achieving complete clearance (grade 0), and only 5.4% remaining in grade 3 (Table 2).

Therapeutic response differed significantly between modalities ($\chi^2 = 44.96$, $p = 0.0001$). On the PRP side, most patients showed only mild response (73.0%), with 16.2% achieving moderate response, 10.8% showing no response, and no cases of good or complete response. In contrast, the PRF side demonstrated superior outcomes, with 29.7% achieving moderate response, 16.2% good response, and 10.8% complete response; mild response was observed in 51.4%, and only 8.1% had no response (Table 3).

Patients' satisfaction differed significantly between treatment modalities ($\chi^2 = 38.4$, $p = 0.0001$). On the PRP side, the majority were moderately satisfied (62.2%), while 29.7% were not satisfied, and only 8.1% were slightly satisfied, with no cases reporting high satisfaction. Conversely, the PRF side showed markedly higher satisfaction, with 62.2% very satisfied, 29.7% moderately satisfied, and 8.1% slightly satisfied; no patients reported dissatisfaction (Table 4).

On the PRP side, no significant correlations were found between treatment response and demographic, clinical, or risk factor variables, as all p-values were > 0.05 (Table 5). Lower eyelid pigmentation showed a significantly better response to PRF treatment compared to pigmentation involving both eyelids ($p < 0.05$). In addition, baseline grade 2 and 3 lesions demonstrated a significantly better response

to PRF compared to grade 4 lesions (p = 0.0001). Otherwise, no significant associations were observed between clinical response to PRF and other demographic, clinical, or risk factor variables (p > 0.05) (Table 6).

Table 1: Demographic, Clinical Characteristics, and Risk Factors of the Studied Group (n = 37)

Variables	Mean ± SD / Median (Range)	n	%
Demographic Data			
Age (years)	**33.1 ± 8.7 (20–51)**		
Gender			
- Female		**24**	**64.9**
- Male		**13**	**35.1**
Occupation			
- Housewife		**9**	**24.3**
- Workers		**28**	**75.7**
Clinical Data			
Disease duration (years)	**4.6 ± 3.4; Median: 4 (0.25–15)**		
Skin phototype			
- I		**2**	**5.4**
- II		**10**	**27.0**
- III		**23**	**62.2**
- IV		**2**	**5.4**
Lesion characters			
- Hyperpigmentation		**37**	**100.0**
- Shade		**6**	**16.2**
- Vascular		**5**	**13.5**
Site of lesions			
- Both eyelids		**11**	**29.7**
- Lower eyelid only		**26**	**70.3**
Family history			
- Negative		**24**	**64.9**
- Positive		**13**	**35.1**
Risk Factors			
Stress		**10**	**27.0**
Insomnia		**9**	**24.3**
Glasses (refractive errors)		**8**	**21.6**
Long TV watching		**8**	**21.6**
Use of cosmetics		**4**	**10.8**
Smoking		**2**	**5.4**

SD: Standard deviation. Notes: Data are expressed as mean ± SD (range), median (range), and frequency (n, %).

Table 2: Grade of Lesions Before and After Treatment on Both Sides (n = 37)

Grade of Lesion	PRP Side n (%)	PRF Side n (%)	χ^2	p-value
Before Treatment				
Grade 2	2 (5.4)	2 (5.4)		
Grade 3	16 (43.2)	16 (43.2)	–	–
Grade 4	19 (51.4)	19 (51.4)		
After Treatment				
Grade 0	0 (0.0)	4 (10.8)		
Grade 1	3 (8.2)	24 (64.9)	36.17	0.0001*
Grade 2	18 (48.6)	7 (18.9)		
Grade 3	14 (37.8)	2 (5.4)		
Grade 4	2 (5.4)	0 (0.0)		

P1 (marginal homogeneity test): 0.0001* (for both PRP and PRF sides)
PRP: Platelet-rich plasma, PRF: Platelet-rich fibrin, χ^2: Chi-square test, SD: Standard deviation. *p < 0.05 considered statistically significant.

Table 3: Therapeutic Response of Treatment Modalities (n = 37)

Therapeutic Response	PRP Side n (%)	PRF Side n (%)	χ^2	p-value
Complete response	0 (0.0)	4 (10.8)		
Good response	0 (0.0)	6 (16.2)		
Moderate response	6 (16.2)	11 (29.7)	44.96	0.0001*
Mild response	27 (73.0)	19 (51.4)		
No response	4 (10.8)	3 (8.1)		
Overall Test				

PRP: Platelet-rich plasma, PRF: Platelet-rich fibrin, χ^2: Chi-square test. *p < 0.05 considered statistically significant

Table 4: Patients' Satisfaction with Treatment (n = 37)

Patients' Satisfaction	PRP Side n (%)	PRF Side n (%)	χ^2	p-value
Very satisfied	0 (0.0)	23 (62.2)		
Moderately satisfied	23 (62.2)	11 (29.7)		
Slightly satisfied	3 (8.1)	3 (8.1)	38.4	0.0001*
Not satisfied	11 (29.7)	0 (0.0)		
Overall Test				

PRP: Platelet-rich plasma, PRF: Platelet-rich fibrin, χ^2: Chi-square test. *p < 0.05 is considered statistically significant.

Table 5: Relationship Between Clinical Response and Various Demographic and Clinical Variables on the PRP Side (n = 37)

Variables	Moderate Response (n = 6)	Mild Response (n = 27)	No Response (n = 4)	f / χ^2 / K	p-value
Age (years)	32.3 ± 8.6	32.8 ± 9.2	36.8 ± 5.7	0.383 (f)	0.685
Disease duration (years)	4.5 (0.6–10)	4 (0.25–15)	3.5 (3–6)	0.003 (K)	0.999
Sex				0.232 (χ^2)	0.890
- Female	4 (66.7)	17 (63.0)	3 (75.0)		
- Male	2 (33.3)	10 (37.0)	1 (25.0)		
Occupation				0.230 (χ^2)	0.891
- Housewife	1 (16.7)	7 (25.9)	1 (25.0)		
- Workers	5 (83.3)	20 (74.1)	3 (75.0)		
Skin phototype				5.36 (χ^2)	0.499
- I	0 (0.0)	2 (7.4)	0 (0.0)		
- II	1 (16.7)	9 (33.3)	0 (0.0)		
- III	4 (66.7)	15 (55.6)	4 (100.0)		
- IV	1 (16.7)	1 (3.7)	0 (0.0)		
Lesion characters					
- Hyperpigmentation	6 (100.0)	27 (100.0)	4 (100.0)	–	–
- Shade	2 (33.3)	3 (11.1)	1 (25.0)	2.04 (χ^2)	0.360
- Vascular	1 (16.7)	4 (14.8)	0 (0.0)	0.72 (χ^2)	0.790
Site of lesions				1.41 (χ^2)	0.490
- Both eyelids	3 (50.0)	7 (25.9)	1 (25.0)		
- Lower eyelid only	3 (50.0)	20 (74.1)	3 (75.0)		
Family history				1.32 (χ^2)	0.520
- Negative	3 (50.0)	19 (70.4)	2 (50.0)		
- Positive	3 (50.0)	8 (29.6)	2 (50.0)		
Grade of lesion before				3.36 (χ^2)	0.499
- Grade 2	0 (0.0)	2 (7.4)	0 (0.0)		
- Grade 3	1 (16.7)	13 (48.1)	2 (50.0)		
- Grade 4	5 (83.3)	12 (44.4)	2 (50.0)		
Risk factors					
- Stress	1 (16.7)	6 (22.3)	3 (75.0)	5.3 (χ^2)	0.070
- Insomnia	1 (16.7)	8 (29.6)	0 (0.0)	1.89 (χ^2)	0.390
- Glasses	2 (33.3)	6 (22.2)	0 (0.0)	1.59 (χ^2)	0.450
- TV watching	0 (0.0)	7 (25.9)	1 (25.0)	1.97 (χ^2)	0.370
- Cosmetic use	2 (33.3)	2 (7.4)	0 (0.0)	3.96 (χ^2)	0.140
- Smoking	0 (0.0)	2 (7.4)	0 (0.0)	0.78 (χ^2)	0.680

PRP: Platelet-rich plasma, SD: Standard deviation, f: One-way ANOVA test, K: Kruskal–Wallis test, χ^2: Chi-square test. $p \geq 0.05$ considered not significant.

Table 6: Relationship Between Clinical Response and Various Demographic and Clinical Variables on the PRF Side (n = 37)

Variables	Complete Response (n = 4)	Good Response (n = 11)	Moderate Response (n = 19)	Mild Response (n = 3)	f / χ^2 / K	p-value
Age (years)	27.5 ± 7.7	32.3 ± 8.2	34.2 ± 9.3	37.0 ± 7.0	0.888 (f)	0.460
Disease duration (years)	1.2 (0.25–2)	5 (0.3–10)	4 (1–15)	4 (3–6)	6.8 (K)	0.079
Sex					4.095 (χ^2)	0.251
- Female	4 (100.0)	5 (45.5)	13 (68.4)	2 (66.7)		
- Male	0 (0.0)	6 (54.5)	6 (31.6)	1 (33.3)		
Occupation					0.40 (χ^2)	0.940
- Housewife	1 (25.0)	2 (18.2)	5 (26.3)	1 (33.3)		
- Workers	3 (75.0)	9 (81.8)	14 (73.7)	2 (66.7)		
Skin phototype					12.64 (χ^2)	0.180
- I	0 (0.0)	2 (18.2)	0 (0.0)	0 (0.0)		
- II	3 (75.0)	1 (9.1)	6 (31.6)	0 (0.0)		
- III	1 (25.0)	7 (63.6)	12 (63.2)	3 (100.0)		
- IV	0 (0.0)	1 (9.1)	1 (5.3)	0 (0.0)		
Lesion characters						
- Hyperpigmentation	4 (100.0)	11 (100.0)	19 (100.0)	3 (100.0)	–	–
- Shade	1 (25.0)	2 (18.2)	2 (10.5)	1 (33.3)	1.35 (χ^2)	0.710
- Vascular	1 (25.0)	1 (9.1)	3 (15.8)	0 (0.0)	1.19 (χ^2)	0.760
Site of lesions					9.7 (χ^2)	0.021*
- Both eyelids	0 (0.0)	7 (63.6)	4 (21.1)	0 (0.0)		
- Lower eyelid only	4 (100.0)	4 (36.4)	15 (78.9)	3 (100.0)		
Family history					3.86 (χ^2)	0.280
- Negative	2 (50.0)	6 (54.5)	15 (78.9)	1 (33.3)		
- Positive	2 (50.0)	5 (45.5)	4 (21.1)	2 (66.7)		
Grade of lesion before treatment					32.86 (χ^2)	0.0001*
- Grade 2	2 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)		
- Grade 3	2 (50.0)	0 (0.0)	13 (68.4)	1 (33.3)		
- Grade 4	0 (0.0)	11 (100.0)	6 (31.6)	2 (66.7)		
Risk factors						

Variables	Complete Response (n = 4)	Good Response (n = 11)	Moderate Response (n = 19)	Mild Response (n = 3)	f / χ^2 / K	p-value
- Stress	1 (25.0)	2 (18.2)	5 (26.3)	2 (66.7)	2.8 (χ^2)	0.420
- Insomnia	1 (25.0)	4 (36.4)	4 (21.1)	0 (0.0)	1.94 (χ^2)	0.590
- Glasses	0 (0.0)	4 (36.4)	4 (21.1)	0 (0.0)	3.34 (χ^2)	0.340
- TV watching	1 (25.0)	0 (0.0)	6 (31.6)	1 (33.3)	4.41 (χ^2)	0.220
- Cosmetic use	1 (25.0)	1 (9.1)	2 (10.5)	0 (0.0)	1.23 (χ^2)	0.750
- Smoking	0 (0.0)	0 (0.0)	2 (10.5)	0 (0.0)	2.0 (χ^2)	0.750

PRF: Platelet-rich fibrin, SD: Standard deviation, f: One-way ANOVA test, K: Kruskal–Wallis test, χ^2: Chi-square test. *p < 0.05 considered statistically significant; p ≥ 0.05 not significant.

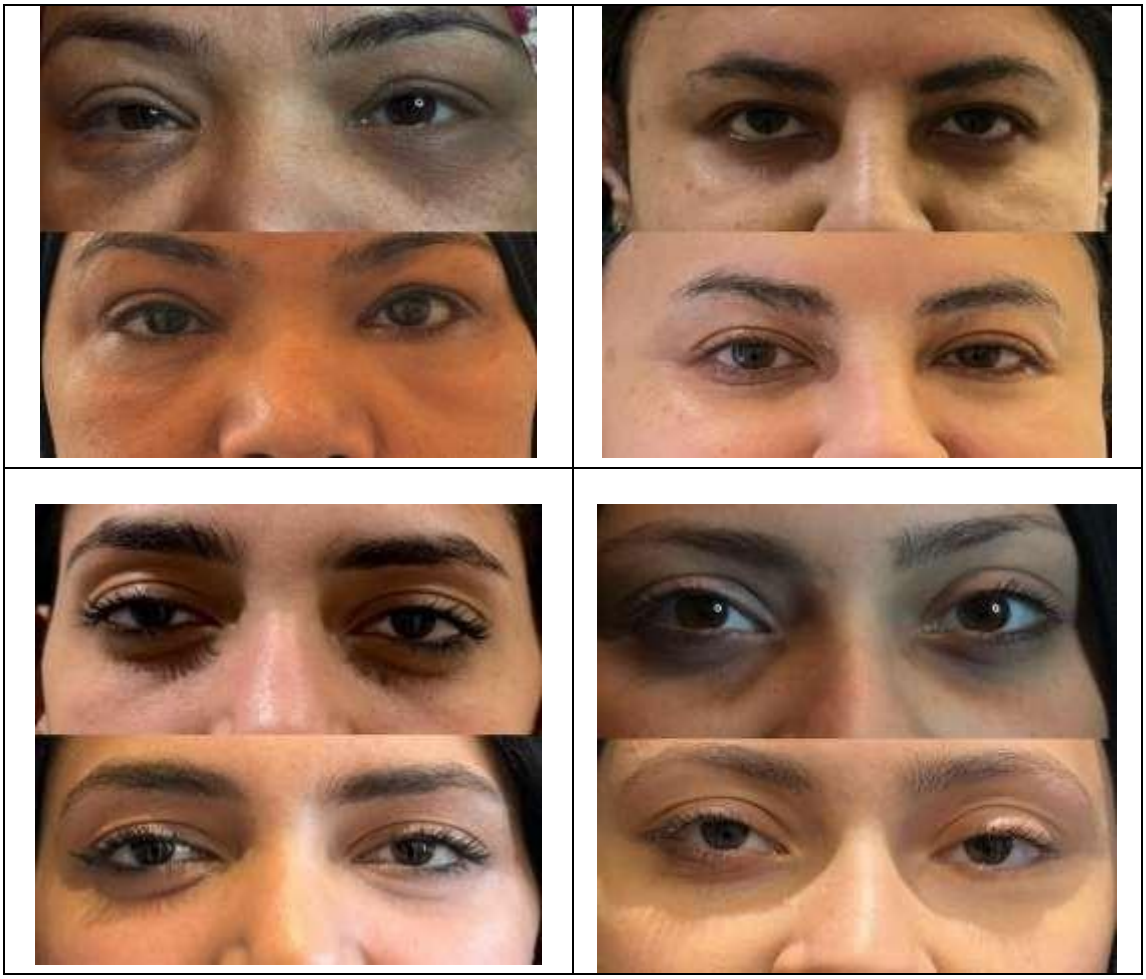

Figure 1: The Right side of the photo managed by PRF and Left side of the photo showing management by PRP: showing Excellent Improvement

DISCUSSION

The POH, commonly referred to as dark circles, is a frequent cosmetic complaint that affects both young and older individuals across all skin types. It influences overall facial appearance and is often associated with an older or tired look. Clinically, it presents as bilateral hyperchromatic macules or patches, most often involving the lower eyelids but sometimes extending to the upper eyelids, malar region, and periocular areas, as described by Goldman et al [15].

The choice of treatment modality depends largely on the underlying etiology. Topical modalities remain widely used, including sunscreens, depigmenting agents, and chemical peels. Ranjan et al [16] highlighted the role of sunscreens and peels, while Dayal et al [17] demonstrated that tretinoin, vitamin C, arbutin, as well as azelaic acid can reduce melanin pigmentation. Laser therapy has also shown value, with Del Duca et al [18] reporting the efficacy of long-pulsed and picosecond lasers in targeting pigment and vascular lesions. Combination regimens using topical agents with lasers appear to improve outcomes further, as noted by Michelle et al [19].

Among minimally invasive options, platelet-rich plasma (PRP) has emerged as a promising technique. Xiao et al. [20] endorsed PRP for facial rejuvenation, while Nanda et al. [21] highlighted its action through angiogenesis, tissue remodeling, stem cell activation, cellular proliferation, and enhanced hyaluronic acid synthesis. Despite these benefits, limitations remain, particularly the requirement for anticoagulants and the rapid growth factor release. To overcome these issues, platelet-rich fibrin (PRF) was introduced, as described by Miron et al. [22] and Kobayashi et al. [23], offering a gradual and sustained release of growth factors without anticoagulant dependency. More recently, injectable PRF, derived from low-speed centrifugation and pioneered by Choukroun and Ghanaati [13], has emerged as a novel approach. Atsu et al. [24] noted that comparative data on PRF versus PRP in dermatology remain scarce, especially for periorbital rejuvenation.

To the best of our knowledge, the current study is the first to compare PRP and PRF in the management of POH. In our series, the patients' mean age was 33.1 years, with the majority being female. This gender predominance aligns with Roberts [25] and Santos et al [26], who also noted a higher frequency of POH among women, likely due to greater concern with cosmetic appearance and healthcare-seeking behavior, as supported by Mendiratta et al [27]. Regarding age distribution, our findings are

consistent with Sheth et al [11], who reported onset typically after puberty and in early adulthood. Comparable mean ages were also described by Sawant and Khan [28] and more recently by Heidari et al [29], supporting the observation that POH tends to affect individuals during early to middle adulthood.

In our study, the disease duration ranged from 3 months to 15 years, with a mean duration of 4.6 years. Most patients had Fitzpatrick skin phototypes II and III, and the lower eyelid was the most commonly affected site. Hyperpigmentation was universal, while shadowing and vascular components were observed in a smaller proportion. A positive family history was documented in more than one-third of patients, confirming the hereditary influence on POH as previously reported by Ranu et al [9] and Strachan and Read [30].

Lifestyle and environmental risk factors were also prominent in our cohort, including stress, insomnia, refractive errors requiring glasses, prolonged screen exposure, and the use of cosmetics. Evans et al [4] described these triggers as part of the multifactorial etiology of POH. Ranu et al [9] reported that over half of affected individuals experienced sleep deprivation, while Jage and Mahajan [31] linked stress to hyperpigmentation through stimulation of the hypothalamic–pituitary–adrenal axis, leading to increased melanocyte-stimulating hormone release. Similarly, Mendiratta et al [27] highlighted the role of cosmetic use, and Chatterjee et al [32] along with David et al [33] demonstrated the impact of sun exposure as a significant risk factor. Together, these findings emphasize the complex interplay of genetic, lifestyle, and environmental influences on POH.

At baseline, non-significant variations were found between the PRP- and PRF-treated sides regarding pigmentation grades, which ensured a fair comparison and reduced bias in evaluating treatment outcomes. Our results revealed a statistically significant improvement in pigmentation severity with PRF compared to PRP ($p=0.0001$). This was accompanied by a superior therapeutic response and greater patient satisfaction on the PRF-treated side, again with high statistical significance ($p=0.0001$). These findings indicate that PRF provided more effective and satisfactory clinical outcomes than PRP in the management of POH.

PRP has long been established as an important modality in aesthetic dermatology due to its rich content of bioactive molecules. Samadi et al [34] emphasized its role in stimulating dermal repair through transforming growth factor-β, which suppresses melanogenesis, and platelet-derived growth factor, which enhances collagen and hyaluronic acid synthesis. This explains its ability to improve skin tone and pigmentation. Its efficacy in hyperpigmentary disorders such as melasma has been demonstrated in the meta-analysis by Zhao et al [35], and Nofal et al [36] reported its benefit in improving POH specifically. More recently, Iranmanesh et al [37] compared PRP with tranexamic acid plus vitamin C mesotherapy and found both modalities to be effective, with no statistically significant difference between them, although PRP showed a slightly higher proportion of good responses.

Importantly, in cosmetic dermatology, patient satisfaction plays a central role in determining treatment success. As noted by Al-Shami [38], perception of improvement directly affects self-image and confidence. In this context, our findings are consistent with those of Gómez et al [39] and Evans et al [4], who demonstrated consistently high satisfaction rates among patients receiving PRP for periorbital rejuvenation.

PRF, as the second generation of platelet concentrates, has been considered superior to PRP in several aspects. Hassan et al [40]

demonstrated that the lower centrifugation speed used in PRF preparation preserves higher levels of platelets, leukocytes, fibrin, and growth factors compared with PRP, thereby enhancing its regenerative capacity. The three-dimensional fibrin matrix of PRF serves as a scaffold that supports platelet entrapment and sustained release of cytokines and growth factors, leading to prolonged biological activity. This fibrin mesh also promotes cellular proliferation, differentiation, and angiogenesis, contributing to tissue remodeling and pigmentation improvement, as reported by Strauss et al [41]. Mahmoodabadi et al [42] further emphasized its role in improving skin hyperpigmentation and overall skin freshness, while Maisel-Campbell et al [43] confirmed long-term benefits in aesthetic applications.

To date, the current work represents the first direct comparison of PRP and PRF in the treatment of POH. Previous comparative studies of PRF and PRP were performed in other clinical fields. Rizk et al [44] compared both scaffolds in regenerative endodontics and found similar outcomes, except for a higher incidence of crown discoloration with PRF. In musculoskeletal indications, Mohi Eldin et al [45] reported superior long-term improvement with PRF compared to PRP in sacroiliac joint dysfunction. Conversely, Li et al [46], in a meta-analysis of randomized controlled trials involving 1440 patients, found that PRP demonstrated more favorable results in rotator cuff repair, whereas PRF showed only modest benefits, suggesting indication-specific differences in their clinical utility. Atsu et al. [24] compared PRP with injectable PRF for facial rejuvenation, reporting marginally superior aesthetic results with PRF, while safety and patient satisfaction remained comparable.

In the current study, baseline demographic and clinical characteristics did not significantly influence the clinical response to either PRP or PRF. However, within the PRF-treated side, patients with lesions confined to the lower eyelid demonstrated significantly greater clinical improvement compared with those who had involvement of both eyelids (p=0.021). Moreover, lesions graded as moderate (grades 2–3) showed superior response to PRF compared with more severe cases (grade 4, p=0.0001). These findings suggest that PRF may be more effective in patients with localized and moderately severe POH. Comparable to our findings, Iranmanesh et al [37] found no significant associations between demographic or clinical risk factors and response to PRP injections, supporting the observation that platelet concentrates exert therapeutic benefit independent of patient background variables.

Among available treatments of all major treatment modalities for periorbital hyperpigmentation, PRP occupies a unique position as a biologic, minimally invasive therapy that addresses both vascular and pigmentary components through dermal remodeling and melanogenesis inhibition. Compared with topical agents or chemical peels, PRP delivers more rapid and often more pronounced improvement with a favorable safety profile. Laser and light therapies can achieve strong pigment clearance but carry higher cost and risk of post-inflammatory hyperpigmentation, particularly in darker skin types common in POH. Fillers and surgical approaches are best suited for purely structural or shadow-related types and do not correct pigmentary changes. In our cohort and in prior systematic reviews, PRP produced significant pigment reduction and high patient satisfaction, confirming it as an effective option for mixed or pigment-dominant POH. Nevertheless, our direct comparison shows that PRF offers superior clinical outcomes and longer growth-factor

activity, suggesting that while PRP remains a valuable therapy, PRF may be the preferred platelet-based modality when available as demonstrated in supplementary Table 1 [4, 6,7,16, 17, 18, 20,21, 22, 35,36].

The current study is one of the novel studies to directly compare PRP and PRF injections for the treatment of periorbital hyperpigmentation. The split-face randomized design minimized inter-patient variability and allowed for objective comparison of both modalities within the same individuals. Blinded assessment of outcomes further strengthened the reliability of the results.

The main limitations were the small sample size and single-center setting, which may reduce the external validity of the results. The follow-up period was short, so long-term durability of the results could not be assessed. Moreover, histopathological evaluation was not performed, which could have provided deeper insight into the mechanisms of improvement.

CONCLUSIONS

Both PRP and PRF were found to be safe modalities for POH management, but PRF demonstrated significantly greater clinical improvement and higher patient satisfaction compared with PRP. These findings suggest that PRF may represent a more effective therapeutic option, particularly in patients with moderate disease severity and lower eyelid involvement. Further larger-scale studies with longer follow-up are recommended to validate these results.

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Authors contributions: A.E.Y. and A.S.A. provided expert oversight throughout the research process, contributing significantly to the conceptual framework and clinical guidance. N.G.M., the corresponding author, was actively involved in patient recruitment, clinical data acquisition, literature review, and drafting of the manuscript. N.G.M. also managed correspondence and ensured coordination between team members during all stages of the study. A.S.A. assisted in data interpretation and critically revised the content for accuracy and depth. A.E.Y. supervised dermatological evaluations and ensured the study adhered to academic standards. All authors reviewed the final manuscript and approved it for publication.

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Table (S1): Treatment Modalities for Periorbital Hyperpigmentation (Dark Circles)

Category / Modality	Mechanism of Action	Key Advantages	Limitations / Adverse Effects	Representative References
Topical agents (hydroquinone, kojic acid, arbutin, azelaic acid, retinoids, vitamin C)	**Reduce melanin synthesis, promote epidermal turnover**	**Widely available, non-invasive**	**Variable efficacy, irritation, need for long-term use**	**[16,17]**
Chemical peels (glycolic, lactic, ferulic, salicylic)	**Exfoliation, melanin dispersion**	**Quick procedure, suitable for pigmentary type**	**Post-inflammatory hyperpigmentation, multiple sessions**	**[16,17]**
Laser & light therapies (Q-switched Nd:YAG, picosecond, pulsed-dye)	**Selective photothermolysis of pigment or vessels**	**Effective for vascular and mixed types**	**High cost, risk of rebound pigmentation**	**[18,19]**
Microneedling / RF microneedling	**Dermal remodeling, collagen induction**	**Improves skin texture, enhances topical**	**Mild downtime, multiple sessions**	**[19]**

Category / Modality	Mechanism of Action	Key Advantages	Limitations / Adverse Effects	Representative References
		penetration		
Carboxytherapy	CO_2 injection → vasodilation, neocollagenesis	Improves vascular congestion	Temporary erythema/edema, repeated sessions	[36]
Fillers (hyaluronic acid)	Correct tear-trough shadowing	Immediate structural correction	Edema, Tyndall effect	[19]
Autologous fat grafting	Volume restoration, growth factors	Durable structural improvement	Donor-site morbidity	[19]
Surgery (blepharoplasty, mid-face lift)	Excises redundant skin/fat, corrects contour	Definitive for structural causes	Invasive, downtime, surgical risks	[19]
Platelet-rich plasma (PRP)	Burst release of platelet-derived growth factors → collagen synthesis, angiogenesis, reduced melanogenesis	Minimally invasive, autologous, improves pigmentation and texture	Requires anticoagulant, rapid GF release, multiple sessions	[4,20,21,35,36]
Platelet-rich fibrin (PRF)	Fibrin scaffold for slow growth-factor release, stem-cell recruitment	Longer bioactivity, no anticoagulant	Limited long-term data	[6,7,22,23]

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