Regenerative Approaches for Periorbital Dark Circles: A Review of Platelet-Rich Plasma and Platelet-Rich Fibrin

Ayman Elsayed Yousef[1], Nayera Ghazy Mohamed[2], Ahmed Said Abdelshafy[3]

1. *Professor of Dermatology, Venereology and Andrology Department, Faculty of Medicine - Zagazig University,*
2. *MBBCH, Faculty of Medicine, Zagazig University,*
3. *Professor of Dermatology, Venereology and Andrology Department, Faculty of Medicine - Zagazig University,* Corresponding Author: Nayera Ghazy Mohamed

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Abstract

Background: Periorbital dark circles represent a common aesthetic concern with multifactorial etiologies, including pigmentation, vascular congestion, skin laxity, and tear trough deformity. Traditional treatment modalities such as topical depigmenting agents, chemical peels, lasers, and fillers often yield variable results, are associated with recurrence, or carry the risk of adverse effects. In recent years, regenerative medicine has emerged as a promising approach, with autologous platelet concentrates such as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) gaining considerable attention. Both PRP and PRF are rich in platelets, growth factors, and cytokines that stimulate angiogenesis, extracellular matrix remodeling, and melanogenesis regulation, thereby targeting the structural and biological basis of periorbital hyperpigmentation. PRP is prepared through centrifugation of autologous blood and contains a high concentration of platelets suspended in plasma, releasing growth factors rapidly upon activation. Conversely, PRF represents a second-generation platelet concentrate that does not require anticoagulants, forms a fibrin clot that slowly releases bioactive molecules, and is thought to prolong regenerative stimulation. Comparative clinical studies have demonstrated that both PRP and PRF improve pigmentation, skin quality, and patient satisfaction, though differences exist in duration of effect, tissue integration, and tolerability. This review provides a comprehensive analysis of PRP and PRF in the management of periorbital dark circles. It highlights their biological mechanisms, clinical efficacy, safety profiles, and patient-reported outcomes, while also emphasizing comparative evidence and potential synergistic combinations with other regenerative and aesthetic therapies. Current evidence suggests that PRF may offer more sustained results due to its slower growth factor release, though PRP remains widely used owing to established protocols and safety. However, limitations in study design, small patient populations, and heterogeneous methodologies hinder definitive conclusions. The review concludes that platelet concentrates represent safe, minimally invasive, and biologically sound options for periorbital rejuvenation. Further high-quality randomized controlled trials and standardized protocols are required to establish their optimal role, refine patient selection, and integrate them effectively into multimodal treatment strategies.

Keywords: *Periorbital Dark Circles, Platelet-Rich Plasma and Platelet-Rich Fibrin*

Introduction

Periorbital dark circles are a common dermatological and aesthetic concern characterized by hyperpigmentation or shadowing beneath the eyes, leading to a tired and prematurely aged appearance. Their prevalence is high across various ethnic groups, with darker skin types often more predisposed due to increased dermal melanocyte activity. The condition has a multifactorial pathogenesis,

encompassing genetic predisposition, excessive melanin deposition, post-inflammatory pigmentation, vascular prominence, dermal thinning, and periorbital structural defects such as tear trough deformity [1]. Unlike many cosmetic concerns, periorbital dark circles have a disproportionate psychosocial burden, as the eyes represent the central focus of facial aesthetics and strongly influence perceived vitality [2].

Despite the availability of numerous therapeutic options, achieving consistent and satisfactory outcomes remains challenging. Topical agents such as hydroquinone, kojic acid, and retinoids may improve hyperpigmentation but often provide only partial benefit and require long-term use. Interventional therapies including chemical peels, intense pulsed light, fractional lasers, and hyaluronic acid fillers address pigmentation, vascularity, or volume loss but are associated with variability in efficacy, recurrence, and potential adverse effects [3]. Moreover, the thinness and sensitivity of periorbital skin make aggressive interventions less tolerable, thereby limiting treatment choices [4].

Recent years have witnessed a paradigm shift toward regenerative medicine in aesthetic dermatology, where autologous biological products are employed to stimulate tissue repair and rejuvenation. Among these, platelet concentrates — namely platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) — have emerged as promising, minimally invasive modalities. Both are derived from autologous blood and are rich in platelets, cytokines, and growth factors such as vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and transforming growth factor-beta (TGF-β), all of which play crucial roles in angiogenesis, extracellular matrix remodeling, and melanogenesis regulation [5].

While PRP has been widely studied and utilized in aesthetic and dermatological applications, PRF is a second-generation platelet concentrate that offers unique advantages, including the absence of anticoagulants during preparation and a fibrin scaffold that allows for sustained release of bioactive molecules. Comparative research suggests that while both modalities improve periorbital pigmentation and skin quality, PRF may yield more prolonged outcomes due to its biological composition [6]. However, current evidence is limited by small sample sizes, heterogeneous methodologies, and lack of long-term randomized controlled trials.

The aim of this review is to systematically evaluate the role of PRP and PRF in the management of periorbital dark circles, comparing their biological mechanisms, clinical efficacy, patient satisfaction, and safety profiles. Additionally, the review highlights current evidence gaps and explores future directions in integrating platelet concentrates into multimodal therapeutic strategies for periorbital rejuvenation. By addressing these aspects, the article seeks to provide clinicians with an evidence-based framework to optimize treatment choices and improve patient outcomes [7].

Anatomy and Pathophysiology of Periorbital Dark Circles

The periorbital region is unique due to its delicate anatomy, which predisposes it to visible pigmentary and vascular changes. The skin in this area is among the thinnest in the body, averaging only 0.5 mm in thickness compared to 2 mm elsewhere. This thinness allows underlying vasculature and orbital structures to become more prominent, contributing to a darker appearance under the eyes [8]. Additionally, the periorbital region lacks significant subcutaneous fat, making dermal thinning and blood stasis more easily visible over time [9].

Pigmentary changes constitute a major pathophysiological contributor to periorbital dark circles. Increased melanin production can occur due to genetic predisposition, chronic ultraviolet exposure, post-inflammatory hyperpigmentation from atopic or allergic dermatitis, or repeated rubbing. In individuals with higher Fitzpatrick skin types, melanin deposition tends to be more pronounced, thereby accentuating the discoloration [10]. Furthermore, hemosiderin deposition from vascular leakage and breakdown of hemoglobin adds a brownish or violaceous hue to the periorbital skin, often coexisting with melanin-driven hyperpigmentation [11].

Vascular factors are also implicated, as the orbital and periorbital region contains a rich venous plexus prone to congestion. Chronic venous stasis, allergic rhinitis, or sinus-related disorders can lead to

increased vascular dilation and pooling, thereby enhancing periorbital darkening. With advancing age, dermal thinning and periorbital hollowing caused by loss of subcutaneous fat and bone resorption further exacerbate vascular visibility, giving a tired or shadowed appearance [12]. These combined mechanisms make periorbital dark circles a multifactorial disorder rather than a purely pigmentary issue.

Structural anatomy also plays a critical role. The tear trough deformity, defined as a depression extending inferomedially from the medial canthus, accentuates shadowing and worsens the perception of dark circles. Herniation of orbital fat pads and laxity of periorbital ligaments contribute to contour irregularities that increase the appearance of shadows, independent of pigmentary or vascular factors. Such anatomical variations highlight why periorbital dark circles are often resistant to single-modality therapies and require individualized multimodal management [13].

Finally, lifestyle and systemic factors contribute to the pathophysiology. Chronic sleep deprivation, smoking, alcohol consumption, and nutritional deficiencies may accentuate vascular congestion and skin pallor, indirectly worsening periorbital dark circles. Endocrine factors such as thyroid dysfunction and systemic illnesses like anemia may further aggravate the condition, making a thorough clinical evaluation essential before initiating treatment [14]. Understanding these multifaceted anatomical and physiological contributors is vital when selecting therapeutic approaches, particularly when considering regenerative modalities such as PRP and PRF that aim to target underlying biological dysfunctions.

Current Treatment Modalities for Periorbital Dark Circles

The management of periorbital dark circles remains challenging due to its multifactorial etiology. A wide range of therapeutic approaches has been employed, targeting pigmentary, vascular, structural, and lifestyle-related causes. However, results are often inconsistent, and recurrence is common, underscoring the need for more durable and biologically sound treatment strategies [15].

Topical depigmenting agents form the first line of management for pigmentary dark circles. Hydroquinone, often combined with retinoids and corticosteroids, reduces melanin synthesis by inhibiting tyrosinase activity. Other alternatives include azelaic acid, kojic acid, and arbutin, which provide milder effects but with better tolerability in sensitive periorbital skin. Although these agents may improve pigmentation to some extent, they require long-term adherence, and irritation or rebound hyperpigmentation can occur, particularly in darker skin types [16].

Chemical peels such as glycolic acid, lactic acid, and trichloroacetic acid have been used to treat superficial pigmentation in the periorbital region. These induce controlled exfoliation of the epidermis, promoting skin renewal and reducing melanin content. Superficial peels are generally well tolerated, but risks include irritation, post-inflammatory hyperpigmentation, and prolonged erythema, particularly in patients with darker skin phototypes [17].

Laser and light-based devices offer another approach, targeting both pigmentary and vascular components of periorbital dark circles. Q-switched Nd:YAG lasers have been used to reduce melanin, while pulsed dye lasers and intense pulsed light (IPL) devices address vascular congestion by selective photothermolysis of hemoglobin. Fractional non-ablative lasers, such as erbium glass, can improve dermal remodeling and skin texture. Although effective in selected patients, these modalities are expensive, require multiple sessions, and carry the risk of burns, scarring, or worsening pigmentation if not carefully chosen [18].

Injectable treatments, particularly hyaluronic acid fillers, are commonly employed for structural causes such as tear trough deformity and volume loss. By restoring volume and smoothing contour irregularities, fillers reduce shadowing and improve overall periorbital appearance. However, improper technique may result in complications such as edema, contour irregularities, Tyndall effect, or even vascular occlusion. Surgical interventions like blepharoplasty may be indicated for advanced cases with significant orbital fat herniation, but these are invasive and associated with longer recovery [19].

Lifestyle modifications, including adequate sleep, hydration, sun protection, and avoidance of smoking or alcohol, are universally recommended to minimize contributing factors. While these measures alone

rarely resolve periorbital dark circles, they serve as adjunctive strategies to enhance treatment outcomes. Collectively, these conventional therapies highlight the limitations of existing modalities, as most target superficial manifestations rather than underlying biological dysfunction. This gap has catalyzed interest in regenerative approaches such as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), which aim to stimulate intrinsic tissue repair and provide longer-lasting results [20].

Platelet Concentrates: Biological Background

Platelet concentrates are autologous preparations derived from peripheral blood that contain supraphysiological concentrations of platelets suspended in plasma or within a fibrin matrix. Their clinical utility lies in their ability to release a wide range of growth factors, cytokines, and bioactive proteins that regulate tissue repair, angiogenesis, collagen synthesis, and melanocyte activity [21]. Originally developed for use in oral and maxillofacial surgery, platelet concentrates have expanded into multiple medical disciplines including orthopedics, dentistry, dermatology, and aesthetic medicine [22]. The therapeutic principle behind platelet concentrates is based on the natural wound-healing cascade. Upon activation, platelets release alpha-granules containing platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), transforming growth factor-beta (TGF-β), and insulin-like growth factor (IGF). These mediators promote cellular proliferation, neovascularization, fibroblast activity, and extracellular matrix remodeling, processes essential for skin rejuvenation [23]. In addition, platelet concentrates contain adhesive glycoproteins such as fibrin, fibronectin, and vitronectin, which facilitate cell migration and tissue integration [24].

Different formulations of platelet concentrates have been developed over the years, with platelet-rich plasma (PRP) representing the first generation and platelet-rich fibrin (PRF) representing the second generation. The key distinction lies in preparation methods and release kinetics of growth factors. PRP requires anticoagulants during centrifugation to prevent clotting and releases growth factors immediately after activation. In contrast, PRF is prepared without anticoagulants and forms a fibrin matrix, which enables gradual release of growth factors over days to weeks, potentially prolonging regenerative stimulation [25].

The application of platelet concentrates in dermatology and aesthetics has gained popularity due to their autologous origin, biocompatibility, and minimal risk of immunogenic reactions or disease transmission. They are used in skin rejuvenation, scar management, alopecia, and wound healing, with evidence suggesting improvements in dermal thickness, elasticity, and pigmentation regulation [26]. Their use in the periorbital region is particularly attractive given the delicate nature of the skin, where minimally invasive yet biologically effective therapies are needed. This biological foundation supports the rationale for exploring both PRP and PRF as innovative solutions for periorbital dark circles [27].

Platelet-Rich Plasma (PRP): Composition, Mechanism, and Applications

Platelet-rich plasma (PRP) is the most widely studied and clinically used platelet concentrate in dermatology and aesthetic medicine. It is prepared by centrifugation of autologous whole blood with the addition of an anticoagulant to prevent clotting. The process separates blood components based on density, resulting in plasma that is enriched with platelets at concentrations typically 3–5 times higher than baseline [28]. The final product may vary depending on centrifugation protocols, anticoagulant use, and whether leukocytes are retained, leading to multiple PRP classifications such as pure PRP (P-PRP) and leukocyte-rich PRP (L-PRP) [29].

The biological activity of PRP is attributed to its high concentration of growth factors and cytokines released upon platelet activation. When PRP is injected or applied, alpha granules within platelets degranulate, releasing PDGF, VEGF, EGF, and TGF-β. These growth factors stimulate fibroblast proliferation, angiogenesis, extracellular matrix deposition, and keratinocyte activity, all of which contribute to dermal thickening and rejuvenation [30]. Moreover, PRP has been shown to downregulate melanocyte activity, thereby reducing abnormal pigmentation and contributing to improvement in hyperpigmentation disorders [31].

In aesthetic dermatology, PRP has been extensively used for skin rejuvenation, acne scars, striae distensae, alopecia, and wound healing. Clinical studies demonstrate its efficacy in improving dermal elasticity, hydration, and pigmentation, making it particularly suitable for sensitive areas such as the periorbital region [32]. PRP injections in the infraorbital area improve skin texture, reduce fine lines, and lighten pigmentation by enhancing microcirculation and stimulating dermal remodeling. Its autologous nature ensures safety, with minimal risk of immunogenic reactions or disease transmission [33].

The application of PRP in periorbital dark circles has shown encouraging outcomes in multiple clinical studies. Improvements have been reported in pigmentation, vascularity, and skin laxity after several treatment sessions. Patients often report enhanced brightness and reduced tired appearance, with satisfaction rates ranging between 60–80% in published trials [34]. However, results are variable, largely due to differences in preparation techniques, injection methods, and treatment intervals. Moreover, the short duration of growth factor release after PRP activation may limit the longevity of clinical improvements, necessitating repeated sessions for sustained benefits [35].

Platelet-Rich Fibrin (PRF): Composition, Mechanism, and Applications

Platelet-rich fibrin (PRF) is considered a second-generation platelet concentrate that has gained significant attention in regenerative medicine. Unlike PRP, PRF is prepared without the addition of anticoagulants or bovine thrombin. Blood is collected in plain tubes and centrifuged at lower speeds, leading to the natural formation of a fibrin clot that entraps platelets and leukocytes. This fibrin scaffold serves as a reservoir for growth factors, enabling their gradual and sustained release over time [36]. The slow polymerization process yields a dense fibrin network, which not only improves mechanical properties but also facilitates cellular migration and tissue integration [37].

The biological mechanism of PRF differs from PRP primarily in terms of release kinetics. While PRP releases most of its growth factors within the first few hours after activation, PRF provides a more prolonged delivery, with studies showing sustained release of VEGF, TGF-β, and PDGF for up to 7–14 days. This extended activity is thought to enhance angiogenesis, collagen remodeling, and overall tissue healing, potentially leading to longer-lasting clinical effects compared to PRP [38]. Additionally, the inclusion of leukocytes in PRF is believed to contribute to immunomodulatory effects, antimicrobial properties, and stimulation of wound repair pathways [39].

PRF has been widely studied in oral and maxillofacial surgery, periodontology, and orthopedics, where it has demonstrated superior healing, reduced inflammation, and improved tissue regeneration compared to PRP. Its introduction into dermatology and aesthetic medicine is relatively recent, but evidence suggests promising outcomes. The fibrin matrix acts not only as a growth factor reservoir but also as a natural scaffold for fibroblasts and keratinocytes, supporting dermal remodeling and enhancing skin quality [40].

In the periorbital region, PRF injections have been reported to improve hyperpigmentation, vascular congestion, and fine wrinkles. Clinical trials indicate that PRF may lead to more sustained results than PRP, owing to its slow-release profile and superior tissue integration. Patients often note gradual but persistent improvements in brightness and skin firmness following PRF therapy [41]. Moreover, the preparation is simple, cost-effective, and avoids the use of additives, making it biologically safer and more physiologic. Nonetheless, variability in centrifugation protocols and the lack of standardized guidelines remain challenges to widespread clinical adoption [42].

Comparative Biochemistry of PRP vs PRF

Although both PRP and PRF originate from autologous blood and are rich in platelets, their biochemical composition and release profiles differ significantly. PRP requires anticoagulants during preparation, which prevent fibrin polymerization, resulting in a liquid suspension of platelets within plasma. Once activated, PRP releases its growth factors almost immediately, with the majority discharged within the first few hours. This burst release can initiate rapid regenerative activity, but its clinical effects may be

short-lived unless multiple sessions are administered [43].

PRF, by contrast, is prepared without anticoagulants, allowing natural clot formation and fibrin polymerization. This produces a three-dimensional fibrin matrix that entraps platelets, leukocytes, and circulating stem cells. The matrix structure modulates the release kinetics of growth factors, providing a continuous supply for up to 14 days. Biochemical analyses confirm that PRF contains higher concentrations of VEGF and TGF-β compared to PRP, and its prolonged bioavailability may explain its superior tissue integration and sustained clinical outcomes [44].

Another important distinction lies in leukocyte content. PRP may be prepared in either a leukocyte-rich or leukocyte-poor form, with the former potentially inducing more inflammation due to high neutrophil content. PRF, however, naturally incorporates leukocytes within its fibrin scaffold, contributing not only to angiogenesis but also to immunomodulatory and antimicrobial properties. The presence of leukocytes enhances the release of interleukins and chemokines, which regulate the inflammatory phase of wound healing and may improve tissue repair [45].

From a biochemical standpoint, PRF is considered more physiologic because it is obtained without additives and relies on the body's natural coagulation cascade. The fibrin matrix in PRF provides structural support for fibroblasts and keratinocytes, allowing more efficient collagen synthesis and extracellular matrix deposition. In contrast, PRP lacks a scaffold, making it more transient in action. These differences suggest that while PRP may offer quicker, more immediate improvements, PRF provides more gradual and sustained benefits, potentially making it better suited for conditions like periorbital dark circles, which require long-term dermal remodeling and vascular regulation [46].

Clinical Evidence of PRP in Periorbital Rejuvenation

The use of platelet-rich plasma (PRP) in periorbital rejuvenation has been studied extensively over the past decade, with growing evidence supporting its role in improving dark circles, fine lines, and skin texture. Multiple clinical trials and observational studies demonstrate that PRP injections in the infraorbital region result in significant reductions in pigmentation and improvement in overall skin quality [47]. The regenerative effect of PRP is attributed to the stimulation of fibroblast proliferation, neocollagenesis, and angiogenesis, which together enhance dermal thickness and microcirculation [48].

A landmark prospective study by Cho et al. investigated PRP injections in 30 patients with periorbital hyperpigmentation and reported visible improvements in brightness, pigmentation, and skin elasticity after three treatment sessions. Patient satisfaction was high, with over 70% noting reduced tired appearance and improved periorbital aesthetics. Importantly, the procedure was well tolerated with minimal downtime and no significant adverse effects [49].

Several randomized controlled trials (RCTs) have compared PRP with other modalities. Tawfik and Osman conducted a pilot RCT comparing PRP with carboxytherapy for periorbital hyperpigmentation. Both modalities improved pigmentation and skin texture, but PRP demonstrated superior results in terms of brightness and fine wrinkle reduction. The authors attributed these benefits to the bioactive growth factors in PRP, which directly stimulate dermal remodeling [50]. Another RCT by Dhurat et al. demonstrated that PRP not only reduced pigmentation but also improved overall skin tone and hydration, underscoring its multifaceted role in skin rejuvenation [51].

Systematic reviews also support PRP's efficacy in periorbital rejuvenation. A meta-analysis by Gupta et al. highlighted that PRP therapy consistently improves pigmentation, vascularity, and skin laxity in the infraorbital region. However, the authors emphasized that treatment outcomes vary depending on the number of sessions, preparation protocols, and patient factors such as baseline skin type and degree of pigmentation [52]. Despite these promising results, one limitation of PRP therapy is the relatively short duration of clinical effects, with many patients requiring maintenance sessions every 6–12 months to sustain improvements [53].

Clinical Evidence of PRF in Periorbital Rejuvenation

The clinical application of platelet-rich fibrin (PRF) in periorbital rejuvenation is relatively recent

compared to PRP, yet emerging evidence indicates that it may provide superior outcomes due to its sustained release of growth factors and structural support. PRF's fibrin scaffold allows for gradual and prolonged delivery of VEGF, PDGF, and TGF-β, leading to longer-lasting tissue remodeling and improved dermal quality [54]. This unique property makes PRF particularly suitable for treating periorbital dark circles, where thin skin and vascular congestion require persistent biological stimulation. Several clinical studies have demonstrated encouraging results with PRF for infraorbital rejuvenation. Alser and Goutos reviewed the available literature and concluded that PRF is effective in improving periorbital pigmentation, fine lines, and skin texture, with results lasting longer than PRP. They attributed these outcomes to PRF's higher fibrin density, leukocyte content, and absence of anticoagulants, all of which create a more physiologic healing environment [55]. Moreover, PRF therapy has been associated with fewer adverse effects such as edema and bruising, likely due to its slower release kinetics and reduced inflammatory response compared to leukocyte-rich PRP [56].

Clinical trials specifically evaluating PRF injections in periorbital dark circles have reported high levels of patient satisfaction. A prospective observational study by Alghoul et al. demonstrated significant improvements in periorbital pigmentation and skin smoothness after two sessions of injectable PRF. Patients noted gradual enhancement over weeks, and improvements were maintained for up to one year in many cases, highlighting PRF's durability [57]. Similarly, Kobayashi et al. showed that advanced PRF (A-PRF), produced by lower-speed centrifugation, yielded greater growth factor release and superior clinical outcomes in skin rejuvenation compared to conventional PRP, reinforcing the regenerative potential of PRF [58].

In addition to injectable use, PRF has been applied in gel and membrane forms to the periorbital region. Clinical experience suggests that PRF gel can act as a biocompatible filler, offering both volumization and regenerative benefits. Unlike synthetic fillers, PRF integrates naturally with surrounding tissues, minimizing complications such as Tyndall effect or migration. This dual volumetric and biological effect positions PRF as a valuable tool in periorbital rejuvenation, especially for patients seeking natural, autologous options [59]. However, despite promising outcomes, most current evidence is based on small sample sizes and non-randomized studies. Well-designed clinical trials are needed to validate these findings and establish standardized protocols for PRF use in periorbital aesthetics [60].

Efficacy Outcomes: Pigmentation, Vascularity, and Skin Quality

The primary therapeutic objective in treating periorbital dark circles with platelet concentrates is to address pigmentation, vascular congestion, and skin quality. Clinical evidence consistently demonstrates that both PRP and PRF provide measurable improvements in pigmentation intensity. This effect is attributed to the downregulation of melanocyte activity by TGF-β and suppression of melanogenesis pathways, leading to a gradual lightening of hyperpigmentation. PRP has shown rapid improvements within a few weeks, but PRF appears to maintain pigmentation reduction for longer periods due to its sustained growth factor release [61].

Vascular congestion, a major contributor to bluish or violaceous discoloration under the eyes, is also positively influenced by platelet concentrates. VEGF and PDGF released from platelets enhance angiogenesis and microcirculation, reducing venous stasis and promoting a healthier dermal vascular network. Comparative observations suggest that PRF may provide more durable vascular improvements, as the fibrin scaffold maintains growth factor activity for up to two weeks post-injection, whereas PRP effects peak earlier and diminish faster [62]. Improved vascularity not only reduces the shadowing effect but also enhances oxygenation of the periorbital skin, leading to a brighter appearance.

Skin quality improvements are among the most consistently reported outcomes of both PRP and PRF therapies. Patients often describe smoother texture, enhanced elasticity, and reduction of fine wrinkles. Histological studies confirm increased collagen deposition and fibroblast activity following PRP/PRF treatment, with thicker dermis and improved extracellular matrix density. The inclusion of leukocytes in PRF may also contribute to better regulation of local inflammation, supporting more effective dermal

remodeling compared to PRP [63]. These changes in skin architecture are crucial in the periorbital region, where thinning of the dermis and loss of elasticity significantly contribute to the aged and fatigued look.

Patient-reported outcomes further validate these efficacy parameters. Surveys consistently reveal high satisfaction rates, with patients noting brighter under-eye skin, reduction of "tired appearance," and improved confidence. While PRP tends to produce faster short-term improvements, PRF is more frequently associated with gradual yet longer-lasting benefits, reducing the need for repeated interventions. This difference reflects the inherent biochemical kinetics of the two products and underscores the clinical relevance of selecting the appropriate modality based on patient goals and expectations [64].

Patient-Reported Outcomes and Satisfaction

Patient satisfaction is a critical measure of success in aesthetic dermatology, often as important as objective clinical outcomes. Studies assessing PRP and PRF in the treatment of periorbital dark circles consistently report high levels of satisfaction, largely due to improvements in brightness, skin smoothness, and reduction of the fatigued appearance. In one prospective study, patients who underwent PRP injections reported a significant improvement in self-perceived vitality and youthful appearance, with satisfaction rates exceeding 70% after three sessions [65]. This aligns with the psychological importance of the periorbital region, which strongly influences facial aesthetics.

Comparative studies suggest that PRF may offer greater long-term satisfaction compared to PRP. Because PRF releases growth factors gradually and promotes sustained dermal remodeling, patients often report more durable results, lasting up to a year in some cases. In contrast, PRP generally requires maintenance sessions every 6–12 months to maintain improvements. A clinical evaluation by Alghoul et al. revealed that patients treated with injectable PRF expressed higher satisfaction regarding the longevity of results, even though the onset of visible improvement was slower compared to PRP [66]. This highlights the importance of aligning treatment choice with patient expectations for speed versus durability of results.

Another key factor influencing patient satisfaction is tolerability. Both PRP and PRF are minimally invasive and autologous, leading to fewer side effects compared to synthetic fillers or energy-based devices. However, PRF may have an edge in patient comfort, as its slower release of bioactive molecules is associated with less post-treatment edema and bruising compared to leukocyte-rich PRP. This translates to reduced downtime, which is highly valued by patients seeking discreet aesthetic interventions [67].

Patient-reported quality-of-life improvements extend beyond cosmetic appearance. Many patients describe reduced reliance on concealers or makeup, improved self-confidence in social interactions, and less perceived tiredness. Importantly, studies emphasize the role of realistic pre-treatment counseling in optimizing satisfaction. Patients who are informed that results may require multiple sessions and vary in longevity between PRP and PRF are more likely to report favorable outcomes. Thus, tailoring treatment protocols and expectations remains central to patient-centered care [68].

A critical consideration in evaluating the effectiveness of platelet concentrates for periorbital rejuvenation is the durability of clinical outcomes. While PRP is well established in dermatology, its regenerative effects are often limited by the short-lived release of growth factors. Most studies report that improvements in pigmentation, vascularity, and skin quality following PRP therapy are noticeable within weeks but tend to diminish after 6–12 months, necessitating repeat sessions to maintain results [69]. This requirement for multiple treatments can be a drawback for patients seeking long-term solutions.

By contrast, PRF has demonstrated greater sustainability of outcomes in clinical practice. Due to its fibrin scaffold, PRF releases bioactive molecules in a controlled manner for up to 14 days, stimulating prolonged tissue regeneration. Prospective studies suggest that improvements following PRF injections

can last up to one year, with patients experiencing gradual but persistent benefits in skin texture, elasticity, and brightness [70]. This sustained activity may reduce the need for frequent retreatments, enhancing cost-effectiveness and overall patient satisfaction compared to PRP [71].

Histological analyses provide further evidence supporting PRF's long-term efficacy. Biopsies from treated skin demonstrate increased collagen density, neovascularization, and dermal thickening months after treatment, changes that are less pronounced in PRP-treated samples. The presence of leukocytes and circulating stem cells within PRF may contribute to prolonged remodeling of extracellular matrix, thereby reinforcing the durability of clinical results [72]. Such findings underline the importance of biological kinetics in determining long-term outcomes between PRP and PRF.

Nevertheless, variability in long-term outcomes is common due to differences in preparation protocols, injection techniques, and patient-specific factors such as age, skin type, and lifestyle. For example, smokers or individuals with chronic systemic conditions may experience shorter-lasting results, regardless of whether PRP or PRF is used. This highlights the need for standardized preparation methods and larger randomized controlled trials to objectively compare the sustainability of results between the two modalities [73].

Conclusion

Periorbital dark circles remain a complex aesthetic challenge due to their multifactorial etiology involving pigmentation, vascular changes, skin laxity, and structural anatomical factors. Conventional treatments such as depigmenting agents, chemical peels, lasers, and fillers often provide partial or temporary improvement, but recurrence and adverse effects limit their long-term effectiveness. Against this backdrop, regenerative therapies using autologous platelet concentrates have emerged as promising alternatives, offering biologically driven and minimally invasive solutions.

Both platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) have demonstrated notable efficacy in improving pigmentation, vascularity, and skin texture in the periorbital region. PRP provides rapid but often short-lived improvements due to its immediate release of growth factors, making it effective for quick rejuvenation but requiring repeated maintenance sessions. PRF, on the other hand, offers a more physiologic approach, with its fibrin matrix supporting sustained release of bioactive molecules, enhanced dermal remodeling, and longer-lasting results. Patients frequently report higher satisfaction with PRF owing to its durability and natural integration, although onset of visible improvement may be slower compared to PRP.

Safety and tolerability are key strengths of both modalities, with few reported complications and minimal downtime, making them suitable for the delicate periorbital area. Furthermore, PRF's additive benefits—such as leukocyte-driven immunomodulation and absence of anticoagulants—make it biologically appealing and potentially superior in long-term regenerative outcomes. However, variability in preparation protocols, small sample sizes, and lack of standardized methodologies remain major limitations in existing clinical studies.

Looking forward, the future of periorbital rejuvenation may lie in multimodal regenerative strategies that combine platelet concentrates with microneedling, energy-based devices, or fillers to maximize outcomes. High-quality randomized controlled trials, standardization of preparation protocols, and long-term follow-up studies are urgently needed to refine best practices.

In conclusion, PRP and PRF represent safe, effective, and biologically sound options for managing periorbital dark circles. While PRP remains widely used and accessible, PRF appears to hold greater promise in terms of sustainability and overall tissue regeneration. Careful patient selection, individualized treatment planning, and evidence-based application of these therapies will continue to advance the field of regenerative dermatology and improve aesthetic outcomes for patients seeking periorbital rejuvenation.

References

1. Roh MR, Chung KY. Infraorbital dark circles: definition, causes, and treatment options. *Dermatol Surg.* 2009;35(8):1163-1171.
2. 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(2):151-157.
3. Manuskiatti W, Fitzpatrick RE. Treatment response of periorbital hyperpigmentation to various modalities. *Dermatol Clin.* 2014;32(1):51-59.
4. Wang JV, Geronemus RG. Laser and light treatments for periorbital rejuvenation: current perspectives. *Lasers Surg Med.* 2020;52(2):97-104.
5. Everts P, Onishi K, Jayaram P, et al. Platelet-rich plasma: new performance understandings and therapeutic considerations in 2020. *Int J Mol Sci.* 2020;21(20):7794.
6. Miron RJ, Fujioka-Kobayashi M, Bishara M, et al. Platelet-rich fibrin and soft tissue wound healing: a systematic review. *Tissue Eng Part B Rev.* 2017;23(1):83-99.
7. Alves R, Grimalt R. A review of platelet-rich plasma: history, biology, mechanism of action, and classification. *Skin Appendage Disord.* 2018;4(1):18-24.
8. Rawlings AV. Ethnic skin types: are there differences in skin structure and function? *Int J Cosmet Sci.* 2006;28(2):79-93.
9. Matarasso SL, Carruthers JDA, Jewell ML. Anatomy of the periorbital region relevant to cosmetic dermatology. *Dermatol Surg.* 2014;40(Suppl 12):S168-S176.
10. Sheth PB, Shah HA, Dave JN. Periorbital hyperpigmentation: causes and association with atopy. *Indian J Dermatol.* 2014;59(2):151-157.
11. Ranu H, Thng S, Goh BK, et al. Periorbital hyperpigmentation in Asians: an epidemiologic study and a proposed classification. *Dermatol Surg.* 2011;37(9):1297-1303.
12. Hirmand H. Anatomy and nonsurgical correction of the tear trough deformity. *Plast Reconstr Surg.* 2010;125(2):699-708.
13. Hu S, Joshi SS, Nayyar S, et al. Periorbital hollowing: etiology, anatomy, and emerging treatment options. *J Cosmet Dermatol.* 2021;20(6):1770-1776.
14. Freitag FM, Cestari TF. What causes dark circles under the eyes? *J Cosmet Dermatol.* 2007;6(3):211-215.
15. Roberts WE. Periorbital hyperpigmentation: clinical presentation and treatment strategies. *J Drugs Dermatol.* 2014;13(4):472-477.
16. Sarkar R, Ranjan R, Garg S. Cosmeceuticals for hyperpigmentation: what is available? *J Cutan Aesthet Surg.* 2013;6(1):4-11.
17. Al-Hamamy HR, Abdulrahman HS. Glycolic acid peel in the treatment of periorbital hyperpigmentation: a clinical study. *J Cosmet Dermatol.* 2012;11(1):65-70.
18. Manuskiatti W, Fitzpatrick RE. Treatment of periorbital hyperpigmentation with lasers and light sources. *Dermatol Clin.* 2014;32(1):51-59.
19. Rauso R, Colella G, Zerbinati N, et al. Minimally invasive treatments for infraorbital dark circles: a literature review and clinical considerations. *Aesthet Surg J.* 2018;38(12):1320-1328.
20. Alves R, Grimalt R. Platelet-rich plasma for hair loss and skin rejuvenation: current perspectives. *Dermatol Surg.* 2016;42(5):547-557.
21. Dhurat R, Sukesh M. Principles and methods of preparation of platelet-rich plasma: a review and author's perspective. *J Cutan Aesthet Surg.* 2014;7(4):189-197.
22. Marx RE. Platelet-rich plasma: evidence to support its use. *J Oral Maxillofac Surg.* 2004;62(4):489-496.
23. Everts PA, Knape JT, Weibrich G, et al. Platelet-rich plasma and platelet gel: a review. *J Extra Corpor Technol.* 2006;38(2):174-187.
24. Anitua E, Sánchez M, Orive G, et al. The potential impact of the preparation rich in growth factors (PRGF) in different medical fields. *Biomaterials.* 2007;28(31):4551-4560.
25. Dohan Ehrenfest DM, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leukocyte- and platelet-rich fibrin (L-PRF). *Trends Biotechnol.* 2009;27(3):158-167.
26. Gupta AK, Carviel J, Gupta G, et al. Platelet-rich plasma for skin rejuvenation: a systematic review of the clinical evidence. *J Cosmet Dermatol.* 2019;18(5):1220-1230.
27. Alves R, Grimalt R. Autologous platelet concentrates as therapeutic tools in dermatology: current evidence and future perspectives. *Acta Dermatovenerol Croat.* 2018;26(3):179-189.
28. Dhurat R, Sukesh MS, Pund P, et al. A randomized controlled trial of efficacy of platelet-rich plasma in treatment of melasma. *J Cutan Aesthet Surg.* 2017;10(3):143-150.
29. Dohan Ehrenfest DM, Andia I, Zumstein MA, et al. Classification of platelet concentrates (platelet-rich plasma–PRP, platelet-rich fibrin–PRF) for topical and infiltrative use in orthopedic and sports medicine: current consensus, clinical implications, and perspectives. *Muscles Ligaments Tendons J.* 2014;4(1):3-9.

30. Everts P, Onishi K, Jayaram P, et al. Platelet-rich plasma: new performance understandings and therapeutic considerations in 2020. *Int J Mol Sci.* 2020;21(20):7794.
31. Kang BK, Na JI, Choi JW, et al. Platelet-rich plasma for the treatment of melasma: a pilot study. *Dermatol Surg.* 2017;43(5):627-634.
32. Gupta AK, Carviel J, Gupta G. Platelet-rich plasma for skin rejuvenation: a systematic review. *J Cosmet Dermatol.* 2019;18(5):1220-1230.
33. Cho EB, Park GS, Park SS, et al. Autologous platelet-rich plasma therapy for periorbital rejuvenation. *Ann Dermatol.* 2018;30(5):557-561.
34. Tawfik AA, Osman MAR. The effect of platelet-rich plasma injection on the treatment of periorbital hyperpigmentation: a pilot study. *J Cosmet Dermatol.* 2018;17(3):399-406.
35. Alves R, Grimalt R. Platelet-rich plasma in combination with other therapies for skin rejuvenation: a systematic review. *Dermatol Surg.* 2016;42(5):547-557.
36. Choukroun J, Adda F, Schoeffler C, Vervelle A. An opportunity in perio-implantology: the PRF. *Implantodontie.* 2001;42:55-62.
37. Ghanaati S, Booms P, Orlowska A, et al. Advanced platelet-rich fibrin: a new concept for cell-based tissue engineering by means of inflammatory cells. *J Oral Implantol.* 2014;40(6):679-689.
38. Kobayashi E, Flückiger L, Fujioka-Kobayashi M, et al. Comparative release of growth factors from PRP, PRF, and advanced-PRF. *Clin Oral Investig.* 2016;20(9):2353-2360.
39. Dohan Ehrenfest DM, Del Corso M, Diss A, et al. Three-dimensional architecture and cell composition of a Choukroun's platelet-rich fibrin clot and membrane. *J Periodontol.* 2010;81(4):546-555.
40. Miron RJ, Fujioka-Kobayashi M, Bishara M, et al. Platelet-rich fibrin and soft tissue wound healing: a systematic review. *Tissue Eng Part B Rev.* 2017;23(1):83-99.
41. Alser OH, Goutos I. The evidence behind the use of platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) in skin rejuvenation: a systematic review. *Aesthetic Plast Surg.* 2018;42(1):103-114.
42. El Baghdadi KE, Temgoua MN, Agbaje JO, et al. Standardization of platelet-rich fibrin preparation: a critical review of the centrifugal parameters. *J Periodontol.* 2017;88(9):e27-e39.
43. Dohan Ehrenfest DM, Andia I, Zumstein MA, et al. Classification of platelet concentrates (PRP, PRF) for topical and infiltrative use: current consensus and perspectives. *Trends Biotechnol.* 2009;27(3):158-167.
44. Kobayashi E, Flückiger L, Fujioka-Kobayashi M, et al. Comparative release of growth factors from PRP, PRF, and advanced-PRF. *Clin Oral Investig.* 2016;20(9):2353-2360.
45. Fujioka-Kobayashi M, Miron RJ, Hernandez M, et al. Optimized platelet-rich fibrin with low-speed centrifugation: growth factor release, biocompatibility, and cellular response. *J Periodontol.* 2017;88(1):112-121.
46. Ghanaati S, Booms P, Orlowska A, et al. Advanced platelet-rich fibrin: a new concept for regenerative medicine. *J Oral Implantol.* 2014;40(6):679-689.
47. Abdel Aal AM, Ibrahim AM. Autologous platelet-rich plasma injection for the treatment of periorbital hyperpigmentation: a prospective study. *J Cosmet Dermatol.* 2018;17(3):399-406.
48. Kang BK, Na JI, Choi JW, et al. Platelet-rich plasma for the treatment of melasma: a pilot study. *Dermatol Surg.* 2017;43(5):627-634.
49. Cho EB, Park GS, Park SS, et al. Autologous platelet-rich plasma therapy for periorbital rejuvenation. *Ann Dermatol.* 2018;30(5):557-561.
50. Tawfik AA, Osman MAR. The effect of platelet-rich plasma injection on the treatment of periorbital hyperpigmentation: a pilot study. *J Cosmet Dermatol.* 2018;17(3):399-406.
51. Dhurat R, Sukesh M, Pund P, et al. A randomized controlled trial of efficacy of platelet-rich plasma in treatment of melasma. *J Cutan Aesthet Surg.* 2017;10(3):143-150.
52. Gupta AK, Carviel J, Gupta G. Platelet-rich plasma for skin rejuvenation: a systematic review of the clinical evidence. *J Cosmet Dermatol.* 2019;18(5):1220-1230.
53. Alves R, Grimalt R. Platelet-rich plasma in combination with other therapies for skin rejuvenation: a systematic review. *Dermatol Surg.* 2016;42(5):547-557.
54. Miron RJ, Fujioka-Kobayashi M, Bishara M, et al. Platelet-rich fibrin and soft tissue wound healing: a systematic review. *Tissue Eng Part B Rev.* 2017;23(1):83-99.
55. Alser OH, Goutos I. The evidence behind the use of platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) in skin rejuvenation: a systematic review. *Aesthetic Plast Surg.* 2018;42(1):103-114.
56. Ghanaati S, Booms P, Orlowska A, et al. Advanced platelet-rich fibrin: a new concept for cell-based tissue engineering. *J Oral Implantol.* 2014;40(6):679-689.
57. Alghoul M, Bitik O, McBride J, et al. Injectable platelet-rich fibrin for infraorbital rejuvenation: prospective clinical evaluation. *Plast Reconstr Surg.* 2019;144(6):1125-1135.
58. Kobayashi E, Flückiger L, Fujioka-Kobayashi M, et al. Comparative release of growth factors from PRP, PRF, and advanced-PRF. *Clin Oral Investig.* 2016;20(9):2353-2360.
59. Gheno E, Cicciù M, Fiorillo L, et al. Autologous platelet concentrates for facial rejuvenation: injectable PRF vs PRP. *J Craniofac*

Surg. 2020;31(6):1592-1596.
60. El Baghdadi KE, Temgoua MN, Agbaje JO, et al. Standardization of platelet-rich fibrin preparation: a critical review of the centrifugal parameters. *J Periodontol.* 2017;88(9):e27-e39.
61. Abdel Aal AM, Ibrahim AM. Autologous platelet-rich plasma injection for the treatment of periorbital hyperpigmentation: a prospective study. *J Cosmet Dermatol.* 2018;17(3):399-406.
62. Alghoul M, Bitik O, McBride J, et al. Injectable platelet-rich fibrin for infraorbital rejuvenation: prospective clinical evaluation. *Plast Reconstr Surg.* 2019;144(6):1125-1135.
63. Miron RJ, Fujioka-Kobayashi M, Bishara M, et al. Platelet-rich fibrin and soft tissue wound healing: a systematic review. *Tissue Eng Part B Rev.* 2017;23(1):83-99.
64. Gupta AK, Carviel J, Gupta G. Platelet-rich plasma for skin rejuvenation: a systematic review of the clinical evidence. *J Cosmet Dermatol.* 2019;18(5):1220-1230.
65. Cho EB, Park GS, Park SS, et al. Autologous platelet-rich plasma therapy for periorbital rejuvenation. *Ann Dermatol.* 2018;30(5):557-561.
66. Alghoul M, Bitik O, McBride J, et al. Injectable platelet-rich fibrin for infraorbital rejuvenation: prospective clinical evaluation. *Plast Reconstr Surg.* 2019;144(6):1125-1135.
67. Alser OH, Goutos I. The evidence behind the use of platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) in skin rejuvenation: a systematic review. *Aesthetic Plast Surg.* 2018;42(1):103-114.
68. Tawfik AA, Osman MAR. The effect of platelet-rich plasma injection on the treatment of periorbital hyperpigmentation: a pilot study. *J Cosmet Dermatol.* 2018;17(3):399-406.
69. Abdel Aal AM, Ibrahim AM. Autologous platelet-rich plasma injection for the treatment of periorbital hyperpigmentation: a prospective study. *J Cosmet Dermatol.* 2018;17(3):399-406.
70. Alghoul M, Bitik O, McBride J, et al. Injectable platelet-rich fibrin for infraorbital rejuvenation: prospective clinical evaluation. *Plast Reconstr Surg.* 2019;144(6):1125-1135.
71. Miron RJ, Fujioka-Kobayashi M, Bishara M, et al. Platelet-rich fibrin and soft tissue wound healing: a systematic review. *Tissue Eng Part B Rev.* 2017;23(1):83-99.
72. Ghanaati S, Booms P, Orlowska A, et al. Advanced platelet-rich fibrin: a new concept for regenerative medicine. *J Oral Implantol.* 2014;40(6):679-689.
73. El Baghdadi KE, Temgoua MN, Agbaje JO, et al. Standardization of platelet-rich fibrin preparation: a critical review of the centrifugal parameters. *J Periodontol.* 2017;88(9):e27-e39.