

Platelet-Rich Plasma: A Comprehensive Review of Emerging Applications in Medical and Aesthetic Dermatology

ABSTRACT

Platelet-rich plasma (PRP) has been integrated into numerous treatment regimens for medical and aesthetic dermatology. While some of these approaches are well-established, many uses are underreported in the literature. We sought to identify and summarize the emerging dermatologic applications for PRP by conducting a comprehensive PubMed search of studies published between 2000 and 2020. These studies were reviewed to synthesize collection methods, treatment schedule, adverse effects, and the impact of therapy for new and emerging uses for PRP. In general, we identified positive treatment outcomes for skin rejuvenation, scar revision, alopecia, pigmentary disorders, lichen sclerosus, leprosy-induced peripheral neuropathy, plaque psoriasis, and nail disorders. Widely, therapy was well-tolerated and suitable for all reported phototypes. The variations in collection and application sequences make concrete recommendations difficult to discern, underscoring the need for a standardized approach to preparation and treatment methods. We hope this review serves as an outline for new and interesting uses for PRP and will help readers familiarize themselves with this exciting technology for comfortable integration into their practices.

KEY WORDS: Platelet-rich plasmas, PRP, emerging treatments, aesthetic dermatology, medical dermatology

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J Clin Aesthet Dermatol. 2021;14(11):44–57.

In recent years, platelet-rich plasma (PRP) has gained popularity in the field of dermatology. As its name suggests, PRP is composed of concentrated platelets suspended in a solution of plasma. It is produced via centrifugation of whole blood, and its autologous nature suggests an excellent safety profile. Platelets have a well-known biological role in wound repair, and PRP harnesses this innate healing potential in a controlled manner by delivering a supraphysiologic concentration of platelets to target tissues. The concept originated in hematology in the 1970s and has since been safely employed in many medical, surgical, and dental applications.¹ The healing and regenerative effects of PRP make it an attractive treatment modality for a number of dermatologic conditions. In this review, we identify, synthesize, and discuss the current evidence on the applications in medical and aesthetic dermatology for which PRP might be beneficial.

Biologic background and collection summary. Platelets are anucleate cytoplasmic fragments of megakaryocytes. Physiologically, they play a crucial role in primary hemostasis, serving as the “first responders” in wound healing. Upon tissue damage and subendothelial

collagen exposure, platelets adhere to the damaged vessel wall, activate, and aggregate, forming a platelet plug that sets the framework for subsequent thrombus formation and primes the area for healing and repair.

Platelet alpha granules contain bioactive proteins, termed growth factors (GFs), which are exocytosed upon activation and are largely responsible for the regenerative properties of PRP. The principal GFs include vascular endothelial GF, platelet-derived GF, transforming GF (TGF), epidermal GF, fibroblast GF (FGF), and insulin-like GF 1. Together, they exert a wide range of physiologic effects, many of which are attractive for both aesthetic and medical dermatology. For instance, platelet releasate stimulates fibroblast proliferation, migration, collagen synthesis, elastin synthesis, and differentiation into myofibroblasts.^{2–11} These GFs also promote follicular growth, lipogenesis, angiogenesis, and extracellular matrix (ECM) remodeling.^{2,10,12} Therefore, PRP is biologically suited for many dermatologic applications, such as skin rejuvenation, hair restoration, scar revision, and wound healing, among others. This review attempts to clarify whether these perceived benefits on a cellular and molecular level translate into clinical improvement.

FUNDING: No funding was provided for this article.

DISCLOSURES: The authors report no conflicts of interest relevant to the content of this article.

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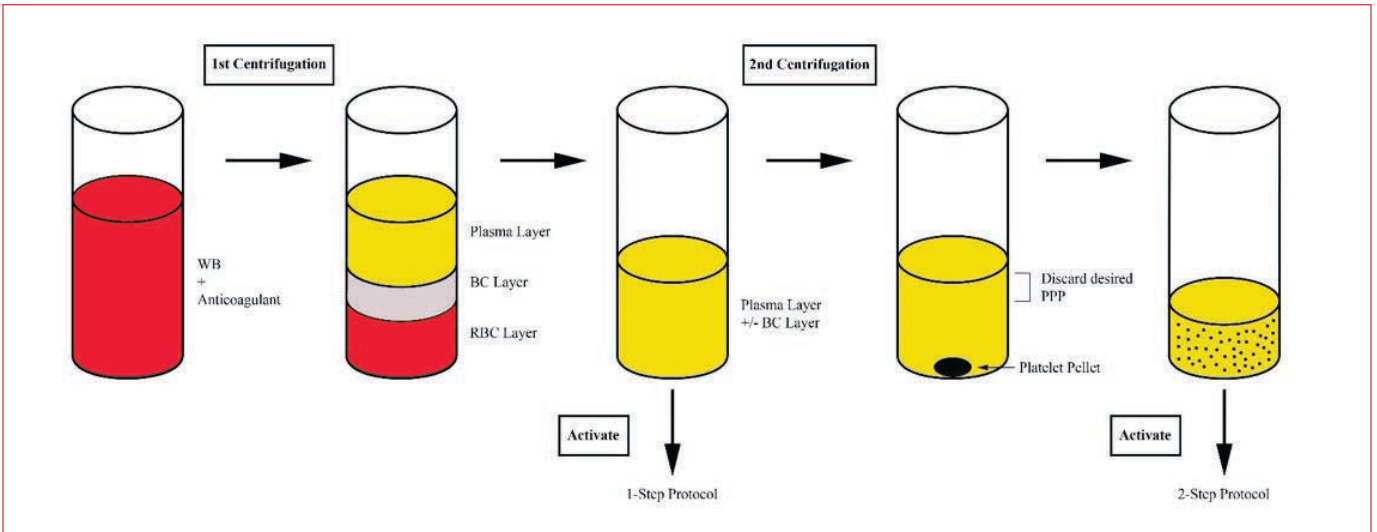


FIGURE 1. The typical process for a one- or two-step PRP preparation protocol. *Abbreviations:* WB, whole blood; BC, buffy coat; RBC, red blood cell; PPP, platelet-poor plasma

A typical PRP preparation consists of the collection of whole blood into a vial prefilled with a citrate-containing anticoagulant, 1- to 2-step centrifugation, the addition of an (often calcium-based) activator, and the application of the product (Figure 1). Centrifugation separates whole blood into layers based on the relative densities of its components. A single spin cycle produces three layers: a lower red blood cell layer, a middle buffy coat layer, and an upper plasma layer. The buffy coat layer contains the leukocytes, so inclusion of this layer in the final PRP product provides a rich leukocyte concentration.^{13–16} Occasionally, the upper plasma layer (with or without the buffy coat) is transferred to a new vial and centrifuged a second time. A portion of the upper platelet-poor plasma is then removed, and the platelet pellet is mechanically resuspended in the remaining solution.¹⁵ Many permutations have been applied to this algorithm, particularly with respect to the addition and type of anticoagulant or activator. These protocol alterations afford a great diversity of PRP products, and some of these varied harvesting methods yield PRP-derived products that have been assigned different titles, such as platelet-rich fibrin (PRF), PRF matrix, and plasma rich in GFs.

METHODS

In order to provide a comprehensive perspective of emerging applications in aesthetic and medical dermatology for which PRP may be useful, we conducted a PubMed search in April 2020 to identify these reports.

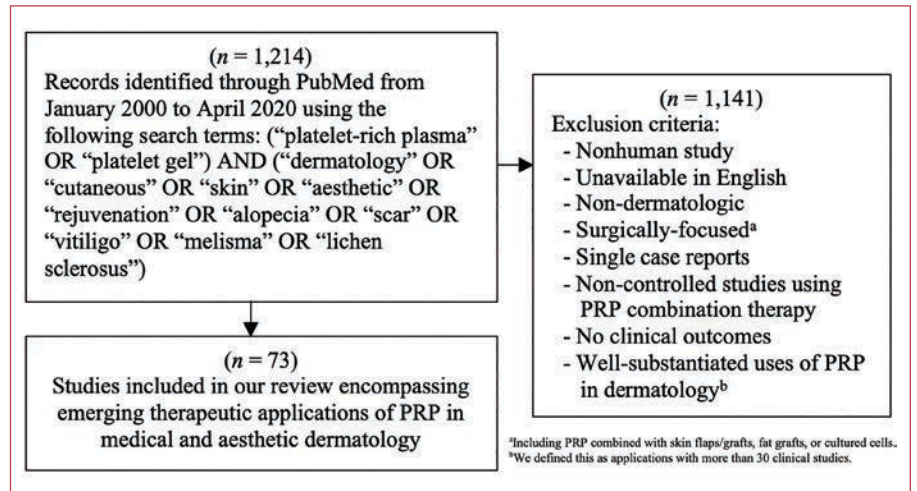


FIGURE 2. Study data-collection method

We utilized a broad review of PRP literature to generate our search terms in order to maximize topics of interest. Our algorithmic approach and exclusion criteria can be found in Figure 2. Controlled and non-controlled studies on PRP monotherapy were included since pre- and post-treatment changes can indicate the efficacy of PRP; however, combination therapy research was only included if the study in question was comparatively controlled and designed so that clinical outcomes could be attributed to the addition of PRP. In an effort to focus more on emerging uses of PRP in dermatology, we identified applications with preliminary clinical literature, which we defined as less than 30 clinical studies. Applications with more than 30 clinical studies, as was the case

for androgenetic alopecia (AGA) and wound healing, were excluded from our comprehensive analysis as their utility is well-substantiated by the literature. These topics will be briefly summarized utilizing recent, comprehensive reviews. For all other applications, we evaluated and compared the available clinical reports ourselves, which included 73 studies. Data acquisition focused on the following details: study design, participant characteristics, PRP preparation parameters, delivery method, treatment schedule, comparisons, and clinical outcomes pertaining to PRP.

Given inherent individual differences and the multiple steps involved in PRP isolation, the final product is prone to high variability. To add complexity, there are inconsistencies in

study caliber, reported parameters, treatment schedules and modalities used, follow-up duration, and measured outcome(s). These factors culminate in immense heterogeneity between studies, so meaningful statistical comparison could not be performed; therefore, this review serves primarily as a qualitative content analysis that compiles, organizes, and consolidates the current evidence for intriguing, novel dermatologic applications of PRP.

RESULTS

Seventy-three studies were included in our review, encompassing treatment modalities for skin rejuvenation, scar revision, alopecia, pigmentary disorders, genital lichen sclerosis, leprosy-induced peripheral neuropathy, plaque psoriasis, and nail disorders. Delivery methods ranged from topical application to intradermal (ID), deep dermal, subdermal, subfollicular, subcutaneous, perineural, and intramatrix injections. Forty-five studies had a treatment group with PRP monotherapy, while 35 studies had a treatment group with PRP in combination with either microneedling ($n=0$ studies), fractional laser resurfacing ($n=17$ studies), subcision ($n=3$ studies), microdermabrasion ($n=1$ study), excimer laser ($n=1$ study), NV-UVB ($n=1$ study), methotrexate ($n=1$ study), or intralesional corticosteroids ($n=1$ study).

Collection and application. The volume of harvested whole blood ranged from 8 to 60 mL, with 65.8% of reports specifying the type of anticoagulant utilized and 1.4% clearly indicating the absence of an anticoagulant. Among the 48 studies that reported an anticoagulant, sodium citrate (including trisodium citrate) and acid citrate dextrose with or without solution A (ACD and ACD-A) were most commonly reported, composing 56.3% and 29.2% of the reported total, respectively. Other anticoagulants reported included ethylenediaminetetraacetic acid, heparin calcium, citrate phosphate dextrose with or without adenine, and citrate dextrose; there was also a single study in which blood was collected into vials prefilled with calcium gluconate and ethanol.¹⁷

Centrifugation speed was reported in 80.8% of studies. Among them, 30.5% performed one centrifugation, while 69.5% completed two cycles. Centrifugation parameters were only compared in studies that reported speeds as multiples of gravity (g), i.e., 61% of all studies.

For one-cycle protocols, centrifugation settings ranged from 70 to $1,200 \times g$ for five to eight minutes, with an average of $637.1 \times g$ for seven minutes. For two-cycle protocols, the first cycle ranged from 110 to $2,000 \times g$ for three to 15 minutes with an average of $585 \times g$ for 8.8 minutes, and the second cycle ranged from 400 to $5,000 \times g$ for 5 to 20 minutes with an average of $1,711 \times g$ for 9.3 minutes. Centrifugation temperature was reported by 8.2% of studies and included 4°C ,¹⁸ 16°C ,¹⁹ 18°C ,²⁰ and 20°C ,¹⁷ and some studies reported a room temperature of 22°C .^{21,22} Of the 36 studies that noted the volume of collected whole blood and resultant PRP volume, the whole blood to PRP yield ranged from 20:1 to 2:1, with an average of 1 mL of PRP produced per roughly 6 mL of whole blood.

The buffy layer was clearly identified in 34.2% of studies, of which 56% included the buffy layer in their final product, while 44% discarded it. An exogenous activator was specified by 58.9% of reports, and 2.7% specified the use of no activator. The most common activators were calcium-based (93% of reported activators), including calcium chloride, calcium gluconate; a single study used calcium bicarbonate.¹⁷ The only identified non-calcium activator was plasma rich in GFs, used in three studies.

Analgesia was utilized in 63% of studies. Among them, topical preparations were employed by 84.8% of providers, with or without occlusion, for durations ranging from 15 minutes to two hours. Other analgesia methods included local anesthesia, nerve block, cold compress, forced-air cooling, distractive devices, and the addition of sodium bicarbonate and lidocaine to the PRP product.

Skin rejuvenation. Twenty-four studies reported PRP use in skin rejuvenation. PRP was used as monotherapy in 19 studies, with fractional laser resurfacing completed in four studies, and with microneedling performed in one study. Of the 19 studies on PRP monotherapy,^{18,23–40} two were randomized controlled trials (RCTs)^{23,40}, four were comparative studies,^{24–27} and 13 were prospective case series.^{18,28–39} PRP monotherapy was employed for soft tissue augmentation or to rejuvenate aged skin. Interventions included topical or ID, deep dermal, subdermal, or subcutaneous injection to the tear troughs, marionette lines, forehead, periocular rhytids, nasolabial folds, midface, neck, or hands. Excluding one-time procedures,

the treatment schedule ranged from two to six sessions with two- to four-week intervals (average of 3.2 sessions with 2.8-week intervals). The sole study on topical PRP monotherapy was applied twice daily for eight weeks.⁴⁰ In all 19 studies, PRP monotherapy showed improvement compared to baseline in at least one clinical outcome, with 13 studies listing significant *P*-values.^{18,23–26,28–29,31,33,35,37–38,40}

Biometric measurements revealed improvements in skin color homogeneity, redness, texture, firmness, wrinkles, pores, elasticity, barrier function, and capacitance compared to baseline.^{25,28,31,34,37} Of 13 studies that evaluated patient-reported outcomes, all noted satisfaction and cosmetic improvements.^{18,23,24,28–32,34,36,37,39–40} Per blinded raters in comparative studies, there was no significant difference in aesthetic outcomes compared to a saline control²³ and ready-made GF mesotherapy,²⁴ PRP was inferior to GF concentrate,²⁶ and PRP was slightly inferior to amnion allograft in subjective improvement of the ogee curve²⁷; however, there were fewer adverse effects noted with the PRP monotherapy treatment compared to either ready-made GF mesotherapy or amnion allograft.^{24,27}

Of the five studies on PRP with fractional laser resurfacing, four were RCTs with inpatient controls,^{41–44} and one was a non-randomized comparative study.⁴⁵ Fractional CO₂ laser (FCL) was used in four studies, while one study used fractional erbium laser.⁴³ Three studies applied topical PRP following laser administration, while single studies performed subcutaneous PRP post-laser⁴² and pre-laser ID PRP injection followed by post-laser topical application.⁴¹ Three studies treated facial skin, while two others evaluated how PRP modulates the healing process when applied to a 1-cm² area on the arm. For two studies with successive treatment sessions, treatment schedules consisted of three sessions with four-week to three-month intervals, and one study performed one FCL treatment session followed by topical application of PRP twice daily for 12 weeks. Compared to controls, the studies reported statistically significant benefits in skin texture, elasticity, wrinkles, or post-procedural erythema and edema. No impact was noted on post-procedural reepithelialization in one study.⁴² In studies noting patient-reported outcomes, all favored the PRP treatment group.^{41–43,45}

El-Domyati et al⁴⁶ conducted a split-face study of 24 patients evaluating PRP combined with

microneedling for skin rejuvenation compared to microneedling alone or with trichloroacetic acid (TCA). The treatment schedule consisted of six sessions separated by two-week intervals. At conclusion, blinded and independent raters assessed photographs with a five-point scale and noted significant improvement in skin wrinkles, texture, and overall satisfaction with the combined PRP and microneedling treatment compared to either microneedling alone or with TCA.

Scar revision. We included 21 studies on PRP for atrophic facial scars. All examined PRP in combination with minimally invasive therapy, stratified as 10 studies considering fractional laser therapy,^{47–56} eight studies considering microneedling,^{21,22,57–62} one study considering microneedling and subcision,⁶³ and two studies considering subcision alone.^{64,65} Most studies targeted atrophic acne scars, apart from two that included post-traumatic and varicelliform scars.^{52,58} Of 17 studies noting participant phototypes, 13 studies reported patient phototypes of III and/or VI.

Of the 10 studies on PRP combined with fractional laser resurfacing, seven were RCTs^{47–51,54,55} and three were comparative studies.^{52,53,56} Apart from one study that evaluated a fractional erbium-doped yttrium aluminum garnet laser,⁴⁷ all studies used an FCL. The combination treatment was completed at the same visit in all studies except one in which PRP and laser therapies were completed on alternating visits.⁴⁷ Application techniques included FCL to the atrophic facial scars, then either percutaneous or topical PRP; 2 to 3 treatments were performed in 3- to 4-week intervals (average of 2.3 sessions with 3.9-week intervals). Eight studies reported statistically significant improvements in scar appearance in the PRP group compared to control,^{47–49,51–55} with seven noting diminished duration and/or severity of post-laser adverse effects (erythema, edema, crusting, oozing).^{48,49,51–54,56} One study revealed significantly worse erythema and edema in the PRP-treated group a few days after therapy, though no significant difference in the duration of these effects was identified.⁵⁰ Gawdat et al⁵⁴ examined FCL in combination with either ID or topical PRP and found both applications significantly enhanced scar appearance compared to FCL alone.⁵⁴ There was no significant difference between the two combinations in regard to the degree of scar improvement, but

the topical PRP group did have a significantly diminished pain score.

Eight studies evaluated the combination of PRP with microneedling, encompassing one RCT⁵⁷ and seven comparative studies.^{21,22,58–62} One study performed percutaneous PRP and microneedling treatments on alternating visits,⁵⁸ and the rest completed the combination treatments at the same visit, performing three to six sessions with two- to four-week intervals (average of 3.9 sessions with 3.3-week intervals). All three studies on percutaneous PRP combined with microneedling showed significant clinical improvement and patient satisfaction with combined PRP and microneedling compared to controls.^{57–59} In one study, there was more severe pain and erythema in the microneedling group than in the ID PRP group.⁵⁸ Topical PRP with microneedling led to mixed results: two studies showed this combination to produce greater clinical improvement than microneedling alone,^{60,61} while one study showed no significant difference between therapies.²² Topical PRP with microneedling produced modest benefits over topical vitamin C with microneedling²¹ and produced no significant difference compared to TCA CROSS (100%).⁶² One study showed significantly less post-procedure erythema and edema with microneedling and topical PRP compared to microneedling alone.²²

Bhargava et al⁶³ RCT evaluated the combination of microneedling with subcision and topical PRP compared to microneedling with subcision alone. Participants received three sessions of their respective treatments in three-week intervals. Upon completion, the PRP group had greater clinical improvement and a shorter duration of post-procedure erythema and edema.

Two studies evaluated the combination of subcision and percutaneous PRP for the treatment of atrophic acne scars.^{64,65} Participants received 3 to 4 monthly sessions of subcision followed by intralesional PRP. Collectively, ID and subcutaneous PRP monotherapy showed significantly greater improvement and fewer adverse effects than subcision combined with PRP. Subcision alone showed the least clinical improvement.

Striae distensae, also known as stretchmarks, are produced via stretching of the skin. They can be erythematous or white, termed striae rubra or striae alba, respectively. Four studies on striae distensae fulfilled our criteria, including two

RCTs,^{66,67} and two comparative studies.^{68,69} These studies evaluated the efficacy of PRP compared to carboxytherapy,^{66,69} tripolar radiofrequency,⁶⁶ tretinoin,⁶⁸ or microdermabrasion⁶⁷ for both striae alba and rubra or striae alba only.⁶⁹ All participants had skin phototype III or VI. The treatment schedule ranged from 3 to 6 sessions of 1- to 4-week intervals (average of 4.5 sessions with 2.6-week intervals). Commonly reported application parameters included 0.1 mL per injection, 1- to 2-cm spacing between injections, and with PRP injected either intradermally or subcutaneously. ID PRP was superior to tretinoin⁶⁸ and microdermabrasion alone.⁶⁷ Regarding the degree of clinical improvement, ID and subcutaneous PRP led to no significant difference compared to carboxytherapy.^{66,69} Regarding patient satisfaction ratings, ID PRP was inferior to carboxytherapy and tripolar radiofrequency.⁶⁶ Erythematous, truncal lesions responded the best to PRP.⁶⁶ All four studies included a treatment group that received PRP monotherapy, and improvement from baseline in all studies was recorded.

One clinical study on the use on percutaneous PRP for keloid scars fulfilled our criteria.⁷⁰ This RCT injected all 40 patients with four sessions of ILC, and, after the last session, also injected the keloids of 20 patients with ID PRP. The PRP group had significant improvement in clinical appearance and diminished post-steroid adverse effects.

Alopecia. We assessed five studies on PRP injections for alopecia areata (AA), including three RCTs,^{71–73} one comparative study,¹⁷ and one case series.⁷⁴ One study focused on patients with alopecia totalis¹⁷; one study included patients with AA, alopecia totalis, and alopecia universalis⁷²; and the rest of the studies examined patients exclusively with AA. Excluding solitary studies, the treatment schedule ranged from 3 to 6 sessions with 2- to 4-week intervals (average of 4 sessions with 3.5-week intervals). Injection details, specified in two studies, included 0.1 mL per injection into the dermis or subfollicular plane with 1- to 2-cm spacing between injections. PRP showed improvement compared to baseline, controls, and standard therapies. Compared to ILC, two studies reported greater hair regrowth and a lower relapse rate with PRP, while there was no significant difference in dystrophic hairs and dysesthesia between the groups.^{71,73} Compared to minoxidil, PRP showed quicker regrowth and decreased

dystrophy and short vellus hairs.⁷²

One article shared two case reports on PRP successfully used to treat cicatricial alopecia.⁷⁵ One patient had central centrifugal cicatricial alopecia with a component of AGA, and the other patient had lichen planopilaris; both received three sessions of 4 to 5 mL of PRP with three-week intervals. Injection depth was not specified. The patients showed global improvement, yet there was regression of improvement noted at six months, suggesting a need for maintenance therapy.

Pigmentary disorders. We reviewed four studies on PRP for non-segmental vitiligo, including three RCTs,^{76–78} and one comparative study.⁷⁹ Patients received 4 to 8 sessions of PRP with 2- to 3-week intervals (average of 6 sessions with 2.5-week intervals). All studies used ID PRP as an adjunct to either FCL,^{76,77} excimer laser,⁷⁸ or narrowband ultraviolet B (NB-UVB).⁷⁹ The excimer and NB-UVB therapy were twice weekly and the FCL was either concurrent with the PRP treatment or every two weeks. PRP injections were placed 0.5 to 2 cm apart, intradermally, with 0.1 mL applied per site. Overall, the combination of PRP with FCL, excimer, or NB-UVB was superior to laser or phototherapy alone. Two studies administered ID PRP alone to a treatment group, and one study found it to be superior to FCL alone,⁷⁶ while the other found it to be inferior to FCL alone.⁷⁷ The face or trunk had the best response to PRP-enhanced treatment,^{76–79} while it was less effective on acral sites.

One RCT on melasma met our inclusion criteria.⁸⁰ This study included 10 female patients with bilateral mixed-type melasma. Patients received four sessions of ID PRP to one half of face and normal saline to the other half with two-week intervals. Biometric measurements demonstrated conflicting results regarding improvements in melanin concentration, although blinded rater review and patient satisfaction was significantly greater on the PRP side. We reviewed three studies on periorbital hyperpigmentation, including one RCT,²⁰ one comparative study,⁸¹ and one case series.³⁷ Patients had 4 to 7 treatment sessions of ID PRP with two-week intervals. Two studies showed significant improvements compared to baseline at 3 to 6 months.^{37,81} Similar to the study on PRP compared to carboxytherapy for striae distensae, PRP did not show significant clinical improvement compared to carboxytherapy.⁸¹ PRP was inferior to a combined TCA 3.75%/lactic acid

15% peel in terms of degree of improvement and patient satisfaction.²⁰

Lichen sclerosus (LS). Six studies on PRP for LS met our criteria, including one RCT⁸² and five case series.^{83–87} Four studies focused on vulvar lesions,^{82,83,86,87} one focused on penile lesions,⁸⁵ and one considered both female and male patients.⁸⁴ Patients received 1 to 6 mL of intralesional (ID, subdermal, or unspecified) PRP for two to 10 sessions with 2- to 12-week intervals (average of 3.2 sessions with 5.5-week intervals), with one study including an additional treatment performed at one year.⁸⁷ For vulvar LS, Goldstein et al initially documented clinical improvement in a case series,⁸⁶ but their subsequent RCT found no improvement compared to a saline control group.⁸² Tedesco et al⁸³ and Behnia-Willison et al⁸⁷ reported decreased vulvar LS lesion count, symptoms, and steroid use in patients treated with PRP. A case series on both vulvar and penile lesions showed improvement compared to baseline in 62% of patients.⁸⁴ For penile LS, one study showed improvement in quality of life scores among all patients, and clinically mitigated resumption of steroids.⁸⁵

Limited applications. There is anecdotal evidence that PRP might be beneficial in a variety of other dermatologic conditions. One RCT displayed that a single perineural injection of PRP significantly improved leprosy peripheral neuropathy.⁸⁸ A prospective comparative trial showed that the combination of intralesional PRP with methotrexate substantially improved patient PASI scores.⁸⁹ Two cases of nail dystrophy (lichen striatus and idiopathic trachyonychia) refractory to topical and/or intramatrix corticosteroids showed improvement after intramatrix PRP injections.¹⁹

Table 1 provides summarized data from reviewed studies showing benefit with PRP therapy. While structured treatment guidelines would be helpful, these are, at this juncture, premature, and this chart merely offers a loose framework for those interested in implementing such therapeutic options in their practices.

DISCUSSION

Collection sequence. Given the abundance of steps involved in producing PRP, it is understandable that there is wide variance in the final products. This is further complicated by the inconsistent reporting of PRP harvesting steps. Our review underscores the need for unified data.

Of the 73 studies we reviewed, 67.1% provided details on anticoagulation, 80.8% reported centrifugation speed(s), 34.2% reported buffy content, 61.6% provided details on activation, and 49.3% reported how much venous blood was collected and how much PRP was produced. This ambiguity makes comparative assessment of results challenging, thereby discrediting the quality of evidence for PRP. Additionally, many seemingly insignificant factors have been suggested to influence final yield, such as tube geometry and venipuncture duration.^{90,91}

Venipuncture methods and anticoagulant use were largely reproduced among studies. While no anticoagulant was clearly superior, our review suggests that ACD or ACD-A or sodium citrate buffers seem to serve as the favored anticoagulants, as they may translate into the highest active platelet concentration. Both of these are citrate-based, which act by chelating calcium. Ethylenediaminetetraacetic acid was historically preferred, but fell out of favor when it was shown to damage platelet membranes.^{15,92–94}

Centrifugation can be represented as multiples of earth's gravitational field (g) or as revolutions per minute (rpm), with the centrifuge rotor radius required to convert between these units.¹⁵ The use of both terms without documenting rotor radius hinders comparison between studies, which is why we are hopeful future studies will consistently report speeds as a measure of "g." Centrifuge speed significantly influences final PRP composition, with high speeds linked to weakened platelet integrity and the risk of pushing platelets into the buffy coat layer resulting in diminished concentration; low speeds may inadequately separate platelets from the cellular layers.^{95–98} The majority of studies utilized two-step centrifugation, composed of an initial "soft spin" to separate the mixture into the red blood cell, buffy coat, and plasma layers; this is followed by a "hard spin," which improves platelet yield by decreasing the plasma volume in which the platelets are suspended.^{96,99,100} The literature reports a very broad range of centrifugation speeds. Research suggests that platelet damage begins to ensue at speeds of greater than 800 g.^{95–97} If this is indeed the case, then it would mean that 28.6% of studies with one-spin protocols and 75.9% of studies with two-step protocols were vulnerable to a loss of platelet integrity. Platelet health is requisite in the final PRP product, as GFs need to exocytose

TABLE 1. Summary of platelet-rich plasma applications which showed benefit, including type of therapy, method of analgesia (if reported), delivery and treatment methods, and level of evidence in accordance with the Evidence-based Medicine modified Grading of Recommendations, Assessment, and Development evidence rating scale^a

APPLICATION	ANALGESIA	DELIVERY METHODS	TREATMENT SCHEDULE	EVIDENCE
Skin rejuvenation				
PRP Monotherapy	Anesthetic cream × 15–60 min, cooling compress, or nerve block	<ul style="list-style-type: none"> ID/DD/SD/SQ PRP to tear troughs, marionette lines, forehead, CF, NLF, midface, neck, or hands <ul style="list-style-type: none"> 25–32-G needle or cannula, 2–6 mL total, 0.02–0.33 mL per injection, 1.5-mm to 1-cm spacing Topical PRP serum to face 	<ul style="list-style-type: none"> 2–6 sessions Q 2–4 weeks (average 3.2 sessions Q 2.8 weeks) Topical PRP serum BID × 8 weeks 	<ul style="list-style-type: none"> Patients noticed a improvement in texture and wrinkles with percutaneous PRP compared to the control side²³ (Grade C) Studies suggest percutaneous PRP provides improvement in wrinkles, elasticity, firmness, texture, pores, tear troughs, color homogeneity, and overall aesthetic appearance compared to baseline^{18,25,26,28,31,33,35,37,38} (Grade B) Topical PRP serum produced improvement from baseline but with no significant difference from serum alone⁴⁰ (Grade D)
PRP Combined with Fractional Laser Resurfacing	Anesthetic cream × 30–60 min	<ul style="list-style-type: none"> ID PRP, then FCL, then topical PPP × 20–30 min to cheek, periorbital area, and forehead ~2.2 mL per ½ face, 0.1 mL per injection FCL or FEL, then topical PRP UO × 20 min to face FCL, then topical PRP <ul style="list-style-type: none"> 3 mL total 	<ul style="list-style-type: none"> 3 sessions Q 4 weeks to 3 months FCL, then topical PRP BID × 12 weeks 	<ul style="list-style-type: none"> Studies suggest PRP combined with fractional laser provides improvement in texture, elasticity, and wrinkles compared to controls^{41,43} (Grade B) Post-laser adverse effects (erythema, edema, pigmentation) were less severe and shorter duration than the controls^{41,42,44} (Grade B)
PRP Combined with Microneedling	Anesthetic cream × 45–60 min	<ul style="list-style-type: none"> MN, then topical PRP <ul style="list-style-type: none"> 600 needles, 1 mm 	<ul style="list-style-type: none"> 6 combined sessions Q 2 weeks 	<ul style="list-style-type: none"> A study suggests PRP combined with MN offers improvement in wrinkles, texture, and overall satisfaction compared to control⁴⁶ (Grade C)
Scar revision				
Atrophic facial scars treated with PRP combined with fractional laser resurfacing	Anesthetic cream × 30–60 min, cooling compress, or forced-air cooling	<ul style="list-style-type: none"> FCL, then ID or topical PRP <ul style="list-style-type: none"> 27–30-G needle, 0.02–0.3 mL per injection, 1–2 cm spacing FEYL and ID PRP alternating 	<ul style="list-style-type: none"> 2–3 sessions Q 3–4 weeks (average 2.3 sessions Q 3.9 weeks) 12 sessions ID PRP Q 2 weeks and 6 sessions FEYL Q 4 weeks 	<ul style="list-style-type: none"> Studies suggest PRP combined with fractional laser provides improvement in smoothness, scar depth, pigmentation, redness, and overall clinical appearance compared to controls^{47–49,51–55} (Grade B) Post-laser adverse effects (erythema, edema, crusting) were less severe and of a shorter duration compared to controls,^{48,49,51–54,56} although one study showed worse adverse effects with PRP⁵⁰ (Grade C) ID vs. topical PRP: no difference in degree of response or downtime, but lower pain score with topical PRP⁵⁴ (Grade C)
Atrophic facial scars treated with PRP combined with microneedling and/or subcision	Anesthetic cream × 30–120 min, cooling compress, or local anesthetic	<ul style="list-style-type: none"> ID/SQ PRP or topical PRP before or after MN PRP injection details: 1–2 mL total, 0.1–0.3 mL per injection, 1-cm spacing <ul style="list-style-type: none"> PRP topical details: 0.5–2 mL total MN details: 192–600 needles, 1.5–2 mm Subcision, then ID/SQ PRP <ul style="list-style-type: none"> 30-G needle, 1.5–3 mL total, 0.1–0.2 mL per injection Subcision, then MN, then topical PRP <ul style="list-style-type: none"> 2 mL total 	<ul style="list-style-type: none"> 2–3 sessions Q 3–4 weeks (average 2.3 sessions Q 3.9 weeks) 3–4 sessions Q 3–4 weeks (average 3.3 sessions Q 3.7 weeks) 	<ul style="list-style-type: none"> Studies suggest PRP combined with MN provides improvement in scar appearance, skin texture, and quality of life compared to controls^{57–59,61} (Grade B) Post-procedure adverse effects (erythema, edema) were less severe compared to control²² (Grade C) Studies suggest PRP combined with subcision provides improvement compared to subcision with or without MN, but ID PRP monotherapy may be superior because it has fewer adverse effects^{63–65} (Grade B)
Striae distensae	Anesthetic cream × 45–60 min	<ul style="list-style-type: none"> ID PRP <ul style="list-style-type: none"> 30-G needle, 2 mL total, 0.1 mL per injection, 1–2-cm spacing ID PRP and MD <ul style="list-style-type: none"> Aluminum oxide/sodium chloride MD system 	<ul style="list-style-type: none"> 3–6 sessions Q 1–4 weeks (average 4.5 sessions Q 2.6 weeks) 	<ul style="list-style-type: none"> Studies suggest PRP provides clinical improvement compared to tretinoin or MD,^{67,68} although there was no significant difference compared to carboxytherapy or tripolar radiofrequency^{66,69} (Grade C) Appears to be most beneficial for striae rubra and truncal lesions⁶⁶ (Grade C)
Keloids	NR	<ul style="list-style-type: none"> ILC, then ID PRP <ul style="list-style-type: none"> 30-G needle 	<ul style="list-style-type: none"> ILC Q 3 weeks, then ID PRP once 	<ul style="list-style-type: none"> A study suggests PRP provides improvement in keloid height, pigmentation, pliability, and overall appearance and reduces post-steroid atrophy and hypopigmentation⁷⁰ (Grade C)

Abbreviations: ID, intradermal; DD, deep dermal; SD, subdermal; SQ, subcutaneous; CF, crow's feet; NLF, nasolabial fold; G, gauge; Q, every; BID, twice per day; FCL, fractional CO2 laser; PPP, platelet-poor plasma; FEL, fractional erbium laser; UO, under occlusion; FEYL, fractional erbium-YAG laser; MN, microneedling; MD, microdermabrasion; NR, not reported; ILC, intralesional corticosteroids; AA, alopecia areata; CCCA, central centrifugal cicatricial alopecia; AGA, androgenetic alopecia; LPP, lichen planopilaris; NB-UVB, narrow-band ultraviolet-B; TCA, trichloroacetic acid; LA, lactic acid; IL, intralesional; PNF, proximal nail fold; LNF, lateral nail fold

^aThe GRADE evidence rating scale we used can be found here: https://www.essential-evidence-plus.com/product/ebm_loe.cfm?show=grade#accept

TABLE 1 (continued). Summary of platelet-rich plasma applications which showed benefit, including type of therapy, method of analgesia (if reported), delivery and treatment methods, and level of evidence in accordance with the Evidence-based Medicine modified Grading of Recommendations, Assessment, and Development evidence rating scale^a

APPLICATION	ANALGESIA	DELIVERY METHODS	TREATMENT SCHEDULE	EVIDENCE
Alopecia				
Alopecia areata	Local anesthetic	<ul style="list-style-type: none"> ID/Subfollicular PRP <ul style="list-style-type: none"> 4 mL per ½ scalp, 0.1 mL per injection, 1.5–2 cm 	<ul style="list-style-type: none"> 3–6 sessions Q 2–4 weeks (average 4 sessions Q 3.5 weeks) 	<ul style="list-style-type: none"> Studies suggest PRP produces more hair regrowth than ILC^{71,73} (Grade B) and produces less hair dystrophy than controls and baseline^{71,73} (Grade B) Does not appear to be beneficial for AA totalis^{17,72} (Grade C)
Cicatricial alopecia	NR	<ul style="list-style-type: none"> ID PRP <ul style="list-style-type: none"> 4–5 mL total 	<ul style="list-style-type: none"> 3 sessions Q 3 weeks 	<ul style="list-style-type: none"> A report suggests PRP produces global hair regrowth CCCA/AGA and LPP; patients would likely benefit from maintenance therapy⁷⁵ (Grade D)
Pigmentary disorders				
Vitiligo	Anesthetic cream × 30–60 min	<ul style="list-style-type: none"> ID PRP with FCL, excimer, or NB-UVB <ul style="list-style-type: none"> 30-G needle, 1 mL total, 0.1 mL per injection, 0.5–2-cm spacing 	<ul style="list-style-type: none"> 6 FCL+PRP sessions Q 2 weeks 4 sessions PRP Q 3 weeks, FCL Q 2 weeks Excimer or NB-UVB twice a week with 6–8 sessions PRP Q 2–3 weeks 	<ul style="list-style-type: none"> Studies suggest PRP combined with either FCL, excimer, or NB-UVB provides improvement in repigmentation compared to laser or phototherapy alone^{76–79} (Grade B)
Melasma	Anesthetic cream × 45 min	<ul style="list-style-type: none"> ID PRP <ul style="list-style-type: none"> 0.1 mL per injection 	<ul style="list-style-type: none"> 4 sessions Q 2 weeks 	<ul style="list-style-type: none"> A study suggests PRP produces improvement in melasma compared to baseline⁸⁰ (Grade C)
Periorbital hyperpigmentation	Anesthetic cream × 60 min	<ul style="list-style-type: none"> ID PRP <ul style="list-style-type: none"> 1 mL total, 0.2–0.3 mL per injection, 2 sites per eyelid, 1-cm spacing 	<ul style="list-style-type: none"> 4–7 sessions Q 2 weeks 	<ul style="list-style-type: none"> Studies suggest PRP provides improvement in color homogeneity compared to baseline³⁷; although there was no significant difference compared to carboxytherapy and was inferior to TCA/LA chemical peel^{20,81} (Grade C)
Lichen sclerosis				
Lichen sclerosis	Anesthetic cream × 30 min or local anesthetic	<ul style="list-style-type: none"> ID/SD PRP <ul style="list-style-type: none"> 27-G needle, 1–6 mL total 	<ul style="list-style-type: none"> 2–10 sessions Q 2–12 weeks (average 3.2 sessions Q 5.5 weeks) 	<ul style="list-style-type: none"> Studies suggest PRP provides improvement in quality of life, overall clinical improvement, number of lesions, symptoms, and steroid use compared to baseline^{85–87} (Grade C)
Other				
Leprosy peripheral neuropathy	NR	<ul style="list-style-type: none"> Perineural PRP <ul style="list-style-type: none"> 1 mL total 	<ul style="list-style-type: none"> Once 	<ul style="list-style-type: none"> A study suggests PRP provides improvement in two-point discrimination⁸⁸ (Grade C)
Psoriasis	NR	<ul style="list-style-type: none"> IL PRP 	<ul style="list-style-type: none"> IL PRP once, then methotrexate for 4 weeks 	<ul style="list-style-type: none"> A study suggests PRP enhances methotrexate therapy for psoriasis⁸⁹ (Grade D)
Nail disorders	Anesthetic cream or vibratory device	<ul style="list-style-type: none"> Intramatrix PRP at two points for each nail <ul style="list-style-type: none"> 2.5 mm proximal and lateral to the junction of PNF and LNF, 0.1 mL per injection 	<ul style="list-style-type: none"> 2 sessions Q 3 weeks 	<ul style="list-style-type: none"> A report suggests intramatrix PRP produces benefit in nail dystrophy¹⁹ (Grade D)

Abbreviations: ID, intradermal; DD, deep dermal; SD, subdermal; SQ, subcutaneous; CF, crow's feet; NLF, nasolabial fold; G, gauge; Q, every; BID, twice per day; FCL, fractional CO2 laser; PPP, platelet-poor plasma; FEL, fractional erbium laser; UO, under occlusion; FEYL, fractional erbium-YAG laser; MN, microneedling; MD, microdermabrasion; NR, not reported; ILC, intralesional corticosteroids; AA, alopecia areata; CCCA, central centrifugal cicatricial alopecia; AGA, androgenetic alopecia; LPP, lichen planopilaris; NB-UVB, narrow-band ultraviolet-B; TCA, trichloroacetic acid; LA, lactic acid; IL, intralesional; PNF, proximal nail fold; LNF, lateral nail fold

^aThe GRADE evidence rating scale we used can be found here: https://www.essentialvidenceplus.com/product/ebm_loe.cfm?show=grade#accept

from platelets to complete their tertiary structure and become bioactive.¹⁰¹ GFs inadvertently released through cell damage impair the product quality and yield underwhelming results.

Including the buffy coat layer (leukocytes) has been actively explored and debated. Leukocyte-rich PRP (L-PRP) might be desired for specific scenarios, such as skin rejuvenation, since it has been shown to produce greater volumization and wrinkle reduction.¹⁰² The proposed positives for L-PRP include synergy between leukocytes and platelets⁴; antimicrobial activity^{103–107}; improved wound healing¹⁰⁶; and the production of MMPs that help modulate angiogenesis, ECM remodeling, and hair cycling.¹⁰⁸ Opponents advocate that L-PRP has catabolic effects via proteases and reactive oxygen species that hinder tissue healing.^{109–111} Further research is needed to help clarify the optimal leukocyte content for specific applications.

It is unclear whether the addition of exogenous activators to PRP benefits application^{15,112} because platelets activate in the presence of endogenous collagen or thrombin.^{93,113,114} Upon initiation of the activation cascade, PRP is most bioactive immediately, with 70% of platelet degranulation occurring within the first 10 minutes and around 95% within the first hour.^{101,115} After this initial release, platelets secrete additional proteins throughout their lifespan (around 5–9 days).^{101,115} Therefore, if using an activator, it is recommended to apply the product within 10 minutes of activation. A dual-syringe mixing system can be used to mix the activator and PRP at the time of application.¹¹⁶ Alternatively, relying on endogenous activation appears to produce a more gradual, sustained release of GFs, which might be beneficial in some clinical settings.^{12,117,118} The most common exogenous activators used in these studies were calcium-based and act by replenishing the calcium chelated during anticoagulation within the collection vial. Some studies have reported the use of thrombin as a common activator.

Other than the study by Doghaim et al,¹⁸ in which their topical PRP product was refrigerated for 90 days, no other studies mentioned storage of PRP. If storage can be successfully employed, this therapy might become even more attractive to patients, as it would hasten the procedure and negate the need for repeated venipuncture. A few studies found that frozen and even lyophilized samples had comparable levels of GFs

when compared to fresh PRP, though the longest freeze time was only three weeks.¹¹⁹ Studies on lyophilized PRP determined that PRP could either be activated before or after freeze-drying¹²⁰ or not activated at all.¹²¹ Further studies on PRP storage are needed.

In 2018, to help formulate consensus recommendations for the research and use of PRP, a working group of 10 experts from the Platelet Physiology Subcommittee of the Scientific Standardization Committee of the International Society on Thrombosis and Haemostasis devised a classification system. Their system distinguishes between PRP and PRF and acknowledges the erythrocyte content (“red” if > 10% erythrocytes), leukocyte content (“L” if > 1% leukocytes), activation status (I, without activation; II, with activation; or III, frozen-thawed preparation), platelet concentration (A, < 900,000/uL; B, 900,000–1,700,000/uL; or C, > 1,700,000/uL), and method of platelet retrieval (1, gravitational centrifugation; 2, standard cell separator; or 3, selective filtration).⁹³ For example, Red-L-PRP IB1 means that the PRP contains greater than 10% erythrocytes, greater than 1% leukocytes, no activation, a platelet concentration of between 900 and 1,700 × 10³, and it was prepared using gravitational centrifugation. If adopted, this nomenclature will make future study methods more transparent. Additionally, precise methodology should be provided in the manuscript to ensure reproducibility. Implementing these details into future literature will afford meaningful comparisons and robust conclusions. Once the reporting of PRP harvesting is standardized, it can then be optimized for specific indications.

Skin rejuvenation. The pathogenesis of skin aging is characterized by the loss of skin thickness, namely due to a reduction in collagen. Histologically, there is thinning of collagen and elastin with reduced density of the ECM, translating into clinical rhytids and visualization of underlying vascular structures.¹²² Fibroblasts are a main target of rejuvenation techniques because they produce collagen, elastin, and other ECM components. Thus, PRP’s stimulatory effect on fibroblast proliferation is an enticing modality for skin rejuvenation.

Skin rejuvenation using PRP monotherapy has reproducibly correlated to an improved appearance of the aged face. Yet, it is inconclusive whether PRP is superior to control therapy or other treatment modalities. ID

injections themselves likely account for a portion of the improvement since skin piercing has a biostimulatory effect, though differences were reported in texture, wrinkles, and skin thickness by patient or biometric measurements when comparing ID PRP to ID saline controls, suggesting that PRP offers a benefit over the injection alone.^{23,25} The skin-rejuvenating effects appear to be subtle, with some studies showing equivocal improvement by objective ratings, yet patients more uniformly reported significant improvement.^{23,24,29} One study on topical PRP monotherapy reported no significant difference compared to control, but the retrieved serum was stored at 4°C for 90 days, potentially diminishing the application effect.⁴⁰

The results for PRP combined with fractional laser therapy strongly suggests that percutaneous or topical PRP might produce synergistic clinical outcomes and reduce post-procedural erythema and edema. Topical PRP also enhanced the clinical efficacy of microneedling. Combination therapy may assist with transepidermal movement of the PRP, though the true explanation is likely more complex as studies investigating microneedling effects have shown conflicting efficacy in promoting molecular penetration.^{123,124} Using fluorescein-stained platelets, one study determined that platelets can navigate almost the entire depth of the microneedle channel when applied at an optimal time of 5 to 30 minutes after microneedling and followed by skin massaging.¹²³ Contrarily, using tattoo dye pigment as an analog for PRP, another study found minimal dermal penetration when applied with microneedling.¹²⁴

In the realm of skin rejuvenation, PRP shows promise as a monotherapy when applied percutaneously, has synergistic effects and diminished downtime when combined with fractional laser resurfacing, and enhances the aesthetic outcomes of microneedling.

Scar revision. PRP’s stimulatory effects on ECM remodeling could account for its potential benefit in scar revision.^{2,3,6,7,125} For the purpose of treating atrophic facial scars, the results strongly favor improved outcomes when PRP is added as an adjunct to laser treatment, microneedling, and subcision. Fewer adverse effects were noted when PRP was combined with all three modalities. For PRP combined with fractional laser therapy, it is debatable whether topical or percutaneous application is more efficacious.

Gawdat et al⁵⁴ noted topical PRP had the same efficacy as ID PRP with a lower pain score, while Faghihi et al⁵⁰ found that ID PRP worsened the severity of post-laser adverse effects but not terminal clinical appearance. Kar et al⁵⁶ found that topical PRP did not improve scar quality compared to laser application alone. Therefore, percutaneous PRP appears to more consistently enhance scar quality but might result in added post-procedural downtime, so the delivery method should be a joint decision between physician and patient. In terms of injection discomfort, a study by Ibrahim et al⁵⁸ reported that ID PRP was significantly less painful than microneedling. ID PRP combined with microneedling showed significant improvement compared to control therapy. The results for topical PRP with microneedling were not as convincing but still favored improvement over microneedling alone and microneedling combined with vitamin C. Three studies evaluating percutaneous PRP monotherapy suggested a positive effect,^{58,62,64} with one study reporting ID PRP to be superior to combination ID PRP and subcision in terms of adverse effects and tolerability.⁶⁴ Collectively, there was a minimal risk of inducing PIH with PRP, supporting its safety in skin of color.^{48,54,62,68,69}

Considering the relatively poor treatment options for striae distensae, percutaneous PRP monotherapy showed improvement compared to baseline and might offer a useful adjunct or alternative for patients who cannot receive or are refractory to standard therapeutic options. ID PRP was superior to other modalities in treating striae rubra, whereas it was equivalent to carboxytherapy or tripolar radiofrequency for managing striae alba.⁶⁶

PRP also benefitted atrophic and keloidal scarring. *In-vitro* and animal models have shown that FGF, released from stimulated platelets, can decrease the scar elevation index by recycling collagen.¹²⁶ Therefore, PRP shows potential as a therapy for hypertrophic and keloidal scars. One study reported that the addition of PRP to ILC treatment of keloids produced significant improvement in keloid characteristics and mollified unwanted steroid effects. Other studies showed benefit with the use of PRP at the surgical margins of excised keloidal tissue, with or without concomitant use of cryosurgery or superficial radiation.^{127–130}

Alopecia. Relative to other dermatologic uses, PRP use for alopecia has a robust body

of evidence, though standardized application guidelines remain limited due to formulary variation in PRP products. In AGA, follicles miniaturize into vellus hairs and prematurely transition to the telogen phase.¹³¹ PRP is believed to promote hair growth by inducing perifollicular angiogenesis, activating anti-apoptotic pathways, prolonging the anagen phase, promoting proliferation of dermal papilla cells, and stimulating differentiation of hair follicle stem cells.^{132–134}

Recent reviews have proposed 3 to 4 monthly injections of PRP followed by maintenance therapy every 2 to 3 months as a treatment schedule for AGA.^{135–138} More frequent treatments are utilized in stubborn disease. While most studies utilize ID delivery,¹⁰⁷ some advocate for subdermal application, which is speculated to improve product diffusion and require fewer injections.^{136,140}

Due to the benefits seen in AGA, many studies have evaluated PRP's role in alopecia areata. AA has a variable disease course, so non-controlled studies require careful interpretation. Some studies have tried to account for this by recruiting patients with recalcitrant AA. PRP showed benefit over baseline, control therapy, minoxidil 5%, and ILC in a variety of outcomes and appears to be a reasonable alternative to ILC.

Cicatricial alopecias eventuate in hair follicle destruction. PRP's ability to stimulate hair growth combined with its remodeling of scarred tissue suggests it might be a helpful therapeutic adjunct for cicatricial alopecias. While the evidence on PRP for cicatricial alopecia is clearly limited by small sample size and lack of objective measurements, it has shown promise in treating lichen planopilaris/frontal fibrosing alopecia and central centrifugal cicatricial alopecia.^{141–144} Additional research is needed to corroborate or challenge these findings.

Pigmentary disorders. Preliminary studies have evaluated the use of PRP in treating disorders, including vitiligo, melasma, and periorbital hyperpigmentation. The theorized molecular mechanism for PRP's utility in both depigmented and hyperpigmented conditions is based on GF melanocyte regulation. TGF- β has been suggested to inhibit melanin synthesis,^{145,146} while FGF promotes melanocyte proliferation and melanogenesis.^{147,148} It is likely that these processes serve to balance melanocyte activity, since PRP has proven useful for conditions with seemingly opposite pathogenic

mechanisms. Nonetheless, clinical research has reported a benefit in both applications. ID PRP shows promise as an adjunct to laser and phototherapies for vitiligo, as a monotherapy for melasma, and as a monotherapy for periorbital hyperpigmentation. The use in vitiligo requires careful follow-up to ensure patients do not Koebnerize.¹⁴⁹

LS. LS is characterized by chronic inflammation, scarring, and atrophy, primarily in the anogenital region. Patients can experience debilitating pruritus, pain, secondary erosions, and adhesions. The gold standard for therapy remain high-potency topical corticosteroids, but that poses an obvious risk when utilized in the genital area. Therefore, alternate effective treatment options would be of great utility. Intralesional PRP has been shown to alleviate symptoms, diminish lesions, reduce steroid use, and improve quality of life in patients with genital LS in five case series. This evidence is encouraging, but a RCT showed no significant difference between ID PRP and ID saline. Additional studies are needed to clarify the efficacy of PRP for LS.

Wound healing. The use of PRP for wound care is intuitive given platelets' physiologic role in initiating post-traumatic healing. Animal and clinical studies have corroborated these theories.¹⁵⁰ PRP has been successfully employed for various wound healing applications, including pressure ulcers,^{151,152} diabetic ulcers,^{153–155} venous leg ulcers,¹⁵⁶ radiation dermatitis,¹⁵⁷ ulcerations of leprosy,^{158,159} refractory lipodermatosclerosis,¹⁶⁰ necrobiosis lipoidica,¹⁶¹ scleroderma ulcers,^{162–164} resistant oral pemphigus vulgaris erosions,^{165,166} graft-versus-host disease oral ulcers,¹⁶⁷ erosive oral lichen planus,¹⁶⁸ pyoderma gangrenosum,^{169–171} ecthyma gangrenosum,¹⁷² ulcerated tophaceous gout,¹⁷³ acquired immunodeficiency syndrome-related crural ulcers,¹⁷⁴ livedoid vasculopathy,¹⁷⁵ and burns.¹⁷⁶

A Cochrane meta-analysis from 2016 evaluated the efficacy of PRP in chronic wound healing and concluded that PRP might improve healing in diabetic foot ulcers, but the evidence for other chronic wounds was unclear.¹⁷⁷ A more recent systematic review on PRP and chronic wounds by Hesseler et al¹⁶ found utility for PRP use in a variety of wounds, suggesting the following treatment regimen for chronic wound healing: activated PRP or leukocyte-rich PRF topically applied 1 to 2 times weekly for 3 to 6 weeks.¹⁶

Adverse effects. Although PRP's autologous nature implies an excellent safety profile, it is not without potential complications. The most notable adverse events included injection site pain in 11 patients^{23,81} and PIH in one patient following microneedling.²¹ Pain was most notable in patients not receiving pre-procedural analgesia,⁸¹ suggesting pain-reducing methods substantially improve tolerability. Otherwise, PRP was well-tolerated, with no severe adverse effects reported. The most commonly reported events included erythema, edema, injection site pain, and bruising. Additional adverse effects included scalp pruritus,¹⁷⁸ transient hair shedding,^{178,179} cervical lymphadenopathy,^{178,180} serum sickness,¹⁸¹ allergic reaction to calcium citrate preparation,¹⁸² cutaneous sarcoidal lesions,^{183,184} and one case of irreversible monocular blindness after glabellar injection.¹⁸⁵ Due to its potential to nourish neoplastic growth, it is advocated to avoid PRP treatment in areas of previous malignancy.^{1,186,187} The efficacy of PRP in patients with active autoimmune disease is equivocal, with some reports cautioning against its use, while others report benefits in this population.¹⁸¹ Interestingly, PRP seems to reduce the effectiveness of neurotoxins.¹⁸⁸

Injection site pain can be minimized with addition of lidocaine,^{27,189,190} bicarbonate,^{27,191,192} or through use of a smaller-gauge needle.²⁷ The type of both anticoagulant and activator may also alter the final solution's pH, with ACD-A and calcium chloride associated with burning due to their low pH.^{193–196} Preparations that use these solutions would benefit from the addition of a bicarbonate buffer to decrease injection-site pain; protocols can also omit anticoagulation or activation altogether.³¹ Tolerability of treatment appears to improve with subsequent sessions.⁷¹

Limitations. Our review has several limitations. To compile a comprehensive overview of current literature for aesthetic and medical dermatologic applications for PRP, we included certain non-controlled and non-randomized studies. Of the 73 total studies included in our review, 29 were RCTs; therefore, 44 studies are inherently prone to selection, reporting, and publication biases. The methods of our review may be subject to selection bias in that we searched a single database and our search terms could have failed to capture some pertinent studies. The reviewed studies had small sample sizes, short follow-up periods, and subjective evaluations; though this was our

methodology for selecting new and emerging applications, it also diminishes the power of this review. The results are not generalizable to all potential candidates of PRP therapy because many reports identified diverse exclusionary criteria. Other major limitations include the formulary variations, inconsistent reporting, and the heterogeneity in clinical outcomes measured, making it difficult to fully evaluate literature.

CONCLUSION

We sought to provide a summarized review of the current evidence regarding the utility of PRP in medical and aesthetic dermatology, focusing on preliminary applications. Most studies reported favorable outcomes. PRP offers a convenient, biocompatible therapeutic option that has not only produced clinical improvement in multiple dermatologic diseases but has improved or mitigated many postprocedural adverse effects. This review underscores the need for robust, randomized, controlled studies to better elucidate the utility of this treatment. We hope this review enforces the need for standardization in future research so that emerging uses for PRP in dermatology can be shared and improved through the collective review of high-quality clinical applications.

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