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REVIEW

Platelet-Rich Plasma and its Use for Cicatricial and Non-Cicatricial Alopecias: A Narrative Review

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ABSTRACT

The concept and description of platelet-rich plasma (PRP) started in the field of hematology and is being extensively used in other fields of medicine. Interest in the application of PRP has been increasing in dermatology, such as in tissue regeneration, wound healing, scar revision, skin-rejuvenating effects, and alopecia. PRP is an autologous blood product containing high concentrations of platelets in a small volume of plasma. Different preparations of PRP may lead to different volumes of PRP, platelet concentration, and presence or absence of leukocytes. PRP is being used as a new therapy for some types of non-cicatricial alopecia such as androgenetic alopecia (AGA) and alopecia areata (AA) and, recently, new insights refer to the possibility of action in the field of cicatricial alopecia, like lichen planopillaris (LPP) and frontal fibrosing alopecia (FFA). This article aims to identify the major indications for the application of PRP in the field of hair disorders, including non-cicatricial and cicatricial alopecia.

Keywords: Alopecia; Alopecia areata; Androgenetic alopecia; Central centrifugal cicatricial alopecia; Cicatricial alopecia; Frontal fibrosing alopecia; Lichen planopillaris; Non-cicatricial alopecia; Platelet-rich plasma

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Key Summary Points

Platelet-rich plasma (PRP) is an autologous blood product containing high concentrations of platelets in a small volume of plasma.

PRP may act at the dermal papilla cells to promote new hair growth, contribute to faster telogen–anagen transition, and increase hair density; good results should be expected with the use of PRP.

In androgenetic alopecia, a positive effect was demonstrated after injections of PRP (mainly after three treatments), showing an increase of hair density in most patients.

The results obtained with the use of PRP in alopecia areata are not so consistent.

PRP might work in some types of cicatricial alopecia, such as lichen planopillaris, central centrifugal cicatricial alopecia, and frontal fibrosing alopecia.

INTRODUCTION

Platelet-rich plasma (PRP) is an autologous blood product containing high concentrations of platelets in a small volume of plasma [1]. The concept and description of PRP started in the field of hematology [2]. Hematologists created the term PRP in 1970s to describe the plasma with a platelet count above that of the peripheral blood and which was initially applied as a transfusion product to treat patients with thrombocytopenia [3]. Ten years later, PRP started to be used in maxillofacial surgery as a platelet-rich fibrin. Fibrin had the potential for adherence and homeostatic properties and PRP with its anti-inflammatory characteristics stimulated cell proliferation [4]. Subsequently, PRP has been used predominantly in the musculoskeletal field in sports injuries. Its use in sports in elite players has drawn widespread media attention and it has been extensively used in this area [5]. Other medical areas that also use PRP are cardiac surgery, pediatric surgery, gynecology, urology, plastic surgery, and ophthalmology [6].

More recently, interest has been increasing in the application of PRP in dermatology, for example, in tissue regeneration, wound healing, scar revision, skin rejuvenating effects, and alopecia [4, 7–13].

PRP, obtained after centrifugation of the blood of the patient, contains an abundance of growth factors (GFs) and cytokines that can affect inflammation, angiogenesis, stem cell migration, and cell proliferation [5, 14–19]. All these factors of PRP would enhance the body's inherent capacity to repair and regenerate. PRP GFs bind with their receptor (GFR) and stimulate protein kinase B (Akt) and extracellular regulated kinase (ERK) signaling. Activation of Akt inhibits two pathways: (1) glycogen synthase kinase-3 beta (GSK3B) that promotes degradation of β-catenin; (2) Bcl-2-associated death promoter (BAD), responsible for inducing apoptosis [20].

Also, PRPs may terminate inflammation by restoring local cells to a non-inflammatory phenotype. This effect could be mediated by various growth factors, including vascular endothelial growth factor (VEGF) and transforming growth factor (TGF), which protects the function of the endothelial barrier [3, 21–24]. So, activated platelets in PRP have the potential to rapidly modify the pericellular microenvironment and accordingly stimulate diverse responses in the nearby milieu [3]. For this reason, PRP application is being used in several fields of medicine. PRP is produced using different methods of platelet concentration via centrifugation and cell separation.

There are many devices worldwide used to produce PRP. The mode of PRP preparation can vary among commercial systems (systems and equipment used for separation, concentration, and plasma collection should meet the applicable quality criteria, EC certified system). Generally, the procedure requires the use of relatively small volumes of blood, obtained from the median cubital vein and drawn into a syringe containing an anticoagulant, such as

sodium citrate. The tubes are centrifuged according to instructions for each device. After being processed, the blood presents in three basic layers: an erythrocyte layer at the bottom of the tube, a PRP layer in the middle of the tube, and a platelet-poor plasma (PPP) layer at the top. After removal of the PPP layer (which represents approximately 3/4 of the supernatant), the PRP is obtained. Immediately before injection into the selected areas, the PRP can be activated or not. The PRP injections may be painful, so the local application of cold before starting the treatment (and after all injections) helps reduce pain. After treatment, no special care is required, and the patient can return to work immediately.

One must consider that different preparations of PRP may lead to different volumes of PRP, platelet concentration, and presence or absence of leukocytes.

Kramer and Keaney [1] performed a study that aimed to identify the various PRP preparation protocols and PRP compositions utilized in clinical trials for the treatment of hair loss. After a systematic review, the authors concluded that there is a lack of regulation of PRP processing methods and of the final composition of the injected product.

The use of PRP in alopecia has been widely studied in recent years. Hair loss encompasses a range of conditions, and different causes can lead to alopecia. Alopecia is divided primarily into non-cicatricial alopecia and cicatricial alopecia. Non-cicatricial alopecias include a number of different types of alopecia with many different causes. These types of alopecia include anagen effluvium, telogen effluvium, androgenetic alopecia, and alopecia areata, among many others.

Cicatricial or scarring alopecia is usually a source of frustration for both the physician and the patient. Some conditions destroy the hair follicle and produce a scar. Other conditions produce permanent alopecia without scar evidence [25].

PRP is being used as a new therapy for some types of non-cicatricial alopecia such as androgenetic alopecia (AGA) [17] and alopecia areata (AA) [26] and, recently, new insights refer to the possibility of action in the field of cicatricial alopecia, like lichen planopilaris (LPP) and frontal fibrosing alopecia (FFA) (Table 1).

METHODS

This article aims to be a comprehensive review regarding the major indications for the application of PRP in the field of hair disorders, including non-cicatricial and cicatricial alopecias. A literature search of records through Medline and PubMed search was conducted to identify studies on PRP use for hair growth in androgenetic alopecia published from 1960 to 2019. Search terms included "platelet-rich plasma" AND "alopecia", "non-cicatricial alopecia", "cicatricial alopecia". Articles not related to platelet-rich plasma and hair disorders were excluded. There were no language restrictions. This article is based on previously conducted studies and does not contain any

Table 1 Indications of platelet-rich plasma in alopecia

Type of alopecia	Clinical indication	Positive response with PRP application	References
Non-cicatricial	Androgenetic alopecia	Yes	[7, 17–19, 27–34]
	Alopecia areata	Yes	[26, 37, 39–41, 44]
	Alopecia areata universalis	No	[46]
Cicatricial	Lichen planopilaris	Yes	[47–50]
	Central centrifugal cicatricial alopecia	Yes	[47]
	Frontal fibrosing alopecia	Yes	[57]

studies with human participants or animals performed by any of the authors.

NON-CICATRICIAL ALOPECIA

Androgenetic Alopecia

One of the first articles regarding the use of PRP in hair diseases was by Uebel et al. [18], in which the authors performed a study in patients undergoing hair transplant surgery. The hair follicular units were embedded in PRP before transplantation. The authors found an improvement of hair growth and an increase in follicular density. The GFs could act upon dermic papilla (DP), leading to intense neovascularization and the progression of new hairs to the anagen phase.

Since then, PRP has started to be considered as a potential therapeutic tool for promoting hair growth, although the precise mechanism by which PRP promotes hair growth is not fully understood [17].

In recent years, several articles [7, 17, 19, 27–32] have been published that refer to the positive effect of the treatment in AGA (Table 2).

Alves and Grimalt [17] performed a clinical trial to access the efficacy of PRP. The results of the randomized placebo-controlled, double-blinded, half-head trial revealed that the administration of PRP led to a significant increase in the mean total hair density, the total terminal hair density, and the number of anagen hairs after 3 months and after 6 months in comparison to the baseline. Also, the anagen/telogen ratio (%) increased, which led to faster telogen-to-anagen transition, as described by Li et al. [7].

Maria-Angeliki et al. [32] published a systematic review to analyze PRP mechanism of action, preparation methods, and therapeutic potential in patients with non-cicatricial alopecia. Among the 14 studies included in their systematic review, they found that PRP could be a possible useful treatment for non-cicatricial alopecia. In most studies, activation and preparation methods were not mentioned, and no standard protocol was employed regarding the frequency of PRP applications.

In 2019, a literature search combined with meta-analysis [33] was used to calculate the overall standardized mean difference in hair density in patients treated with PRP injections in comparison with baseline and placebo treatment. Ten studies in which parameters were considered more scientifically rigorous were included. The results of meta-analysis favor the treatment of PRP when compared with placebo and baseline hair restoration parameters (especially hair density) in AGA monotherapy or adjunct therapy.

Patient characteristics may also influence the results of PRP treatment as stated before by Alves and Grimalt [17], in which they demonstrate a statistically significant association between hair density and patients below 40 years with positive family history of AGA and more than 10 years of duration of the disease. In addition, there was a correlation between anagen hairs and patients older than 40 years and beginning of AGA with age superior to 25 years.

Many of the articles published focus on patients who received treatment with PRP alone. Patients who received topical and/or systemic treatments for AGA in the previous 12 months were typically excluded. Considering that most patients with AGA observed in our clinical practice are undergoing therapy for their alopecia, it is postulated that PRP used in combination could help to achieve better results, especially in patients whose condition appears to stabilized or the improvement is slow.

A clinical trial was designed to assess the efficacy of PRP in combination with 5% minoxidil topical solution and 1 mg finasteride orally administered for the treatment of AGA. The present study included 24 patients with AGA. Patients were instructed to maintain their usual AGA treatment throughout the protocol or were excluded from the study. They received a cycle of three treatments (at a 1-month interval) with PRP on half of the head and saline solution (placebo) on the other half. Follow-up took place after 6 months. On the basis of the obtained data, treatment with PRP in

Table 2 Effects of PRP in different cicatricial and non-cicatricial alopecia

Authors	Study type	Clinical indication	No. patients	Group control	Follow-up (months)	Positive response with PRP	Complications
Alves and Grimalt [17]	RCT	AGA	22	Yes (half-head)	6	Yes	No
Uebel et al. [18]	Prospective nonrandomized	AGA + hair transplantation	20	Yes	7	Yes	No
Cervelli et al. [27]	Retrospective nonrandomized	AGA	10	Yes	12	Yes	No
Takikawa et al. [19]	RCT	AGA	26	Yes	3	Yes	N/A
Schiavone et al. [29]	Prospective nonrandomized	AGA	64	No	6	Yes	No
Jha et al. [49]	Pilot study	AGA	20	Yes	3	Yes	No
Trink et al. [26]	RCT	AA	45	Yes	12	Yes	No
Khademi et al. [46]	Pilot study	AA totalis	10	No	4	No	No
Dina and Aguh [47]	Case series	CCCA/LPP	2	No	3	Yes	No
Bolanča et al. [48]	Clinical case	LPP	1	No	4	Yes	No
Özcan et al. [57]	Clinical case	FFA	1	No	5	Yes	No
Jha [50]	Clinical case	LPP	1	No	–	Yes	No

RCT randomized clinical trial, *AGA* androgenetic alopecia, *AA* alopecia areata, *LPP* lichen planopilaris, *CCCA* central centrifugal cicatricial alopecia, *FFA* frontal fibrosing alopecia

combination with a concomitant medication (topically administered minoxidil or orally administered finasteride) significantly increased the number of hairs, hair density, terminal hair density, and the number of anagen hairs in comparison to baseline and the control side. In addition, patients who received topically administered minoxidil along with PRP showed a greater improvement.

A randomized, controlled, crossover pilot study was performed [34] in order to evaluate the efficacy of PRP in the treatment of AGA when compared with topically administered minoxidil. Twenty female patients were selected and divided into two arms: arm A received PRP injections every 4 weeks for a total of three treatments; then patients underwent an 8-week washout. Thereafter, they received crossover

treatment with minoxidil, applying the 5% foam once daily, for a total of 12 weeks. Patients in arm B were randomized reversed in sequence, first using minoxidil for 12 weeks, followed by an 8-week washout, and then performing the three treatments with PRP. According to the authors, the results of the study suggest that PRP is effective as a treatment for hair regrowth in female AGA, although perhaps not as effective as minoxidil, despite the quality-of-life questionnaire showing a better response after PRP use versus minoxidil.

Lachgar et al. [35] demonstrated that minoxidil stimulates the production of GFs, such as VEGF, in cultured DP cells, and that the effect might promote hair growth. This upregulation of VEGF helps maintain DP vasculature and hair growth [36]. PRP also produces different GFs, leading to intense neovascularization [18] and the increased proliferation of human DP cells [7]. This effect might support the hypothesis that PRP potentiates the effect of minoxidil by promoting the anagen phase and delaying the initiation of the catagen stage. Although more studies are needed and the mechanism is not fully understood, the combination of topically administered minoxidil and PRP appears to lead to a stronger improvement of regrowth.

Thus, one might consider PRP to be safe and effective when used concurrently with the patient's current medication.

Regarding the protocol used in PRP there is no standardization. According to the literature and personal experience, a minimum of three sessions should be performed 1 month apart. Then, at least two or three more sessions should be performed after 6 months to maintain the regrowth [37].

Alopecia Areata

The available articles concerning PRP use and other types of alopecia are sparse. Only a few articles discuss PRP efficacy in patients with alopecia areata (AA). AA is a common non-scarring type of alopecia, which has different clinical presentations, classified according to the hair loss pattern or extent [37]. In some cases, AA is associated with other autoimmune diseases such as vitiligo, atopic dermatitis, diabetes, hypothyroidism, and pernicious anemia [39–41].

There is an unpredictable course of AA regarding the treatment options. Spontaneous regrowth sometimes occurs over several months.

The most common treatments in patients with AA are topical or intralesional corticosteroids (triamcinolone acetonide) and systemic corticosteroids (continuous or as pulse therapy) [42–44]. Several treatment modalities include topically administered minoxidil, topical immunotherapy (squaric acid dibutylester), anthralin, phototherapy, immunosuppressants, and immunomodulators [38].

Trink et al. [26] published the first article regarding treatment with PRP in patients with AA. In 45 randomized patients, some received intralesional injections of PRP, triamcinolone acetonide (TrA), or placebo in one half of their scalp. The other half of the scalp was not treated. After three treatments of PRP in the affected areas, the authors found that the administration of PRP increased hair regrowth in comparison to triamcinolone acetonide or placebo. Also, there was a decreased of the burning or itching sensation after treatment with PRP.

Another article [44] regarding PRP and AA included 20 patients for whom different therapies for AA had proved unsuccessful in the previous 2 years. The patients received a total of six PRP sessions at 1-month intervals. According to the authors, after 1 year of follow-up, only one of the 20 patients had a relapse.

Albalat et al. [41] performed a study to compare the safety and efficacy of PRP versus the injection of intralesional corticosteroids (ILCs) in 80 selected patients with AA. The patients were classified randomly into two groups: group I ($n = 40$) received from three to five sessions of ILCs, one session every 2 weeks; and group II ($n = 40$) received one session of PRP every 2 weeks, for three to five sessions. The authors found significant regrowth of pigmented hair and decrease of dystrophic hair in both groups. The difference between both groups was insignificant, although more relapse was observed with ILCs.

There are many subtypes of AA, such ophiasis form, which affects the occipital and parietal scalp. This form of alopecia usually is more resistant to treatment. Jeff Donovan described a case report [45] of a patient with ophiasis-type alopecia areata, resistant to minoxidil, topical steroids, and three treatment sessions of ILC injections. In this case, after 2 years of no response, the authors administered autologous PRP in the affected areas. PRP led to hair regrowth in the first month with "robust regrowth of hairs measuring 2.8 cm by month 3". The effectiveness of PRP specifically in ophiasis warrants further study.

Another type of alopecia areata is alopecia areata totalis. Khademi et al. [46] published a study with ten patients with clinical diagnosis of AA totalis for at least 3 years who had not received any therapy within 3 months before the beginning of the study. The patients received one single intradermal injection of PRP on the scalp. After 4 months of follow-up, no hair regrowth was seen in eight patients and in two patients only less than 10% hair regrowth was observed. Overall, no significant effect was found for PRP on hair regrowth.

Some studies demonstrated that PRP is effective for the treatment of patients with AA [26] and that PRP could be a valid treatment option for patients with AA, but not for AA totalis, in which no regrowth was noted.

CICATRICIAL ALOPECIA

Recently, some cases have been published about the use of PRP in cicatricial alopecia, such as lichen planopillaris (LPP) and frontal fibrosing alopecia (FFA). There is very little information with only anecdotal cases reported.

Dina and Aguh [47] described two cases of primary cicatricial alopecia (PCA) successfully treated with PRP. The first patient was a 53-year-old woman with biopsy-proven central centrifugal cicatricial alopecia (CCCA) and androgenetic alopecia (AGA). The authors performed three sessions of PRP (1 month apart) after all the previous treatments were proven to be ineffective. After PRP injections, a normal follicular density was noted along the temporal hairline, and there was greater than 50% improvement in hair density along the scalp vertex.

The second patient was a 70-year-old woman with a diagnosis of LPP, confirmed by scalp biopsy. Beside the gradual hair loss, pruritus, and erythema diffusely across the scalp, a loss of eyebrows and hair on the arms, legs, and axillae was noted. As the previous treatments did not lead to any improvement, the authors performed three sessions of PRP at 4 weeks apart. As a result, a normal density was noted diffusely across the scalp and frontal hairline with only minimal residual perifollicular erythema and scaling. No improvement of the eyebrows was noted. According to the authors, a global improvement of hair density in both patients with cicatricial alopecia after administration of PRP was noted.

Lichen planopilaris is classified as a primary lymphocytic cicatricial alopecia whose treatment remains a challenge. Bolanča et al. [48] described a case report of a patient with LPP, confirmed by scalp biopsy, who has failed previous treatments. The authors hypothesized that GFs released by the use of PRP may arrest the development of LPP. They performed treatment with PRP with three consecutive treatments and a 6-month follow-up. Following the treatment, they found that a complete regression of itching and hair shading was achieved with no perifollicular erythema and perifollicular scaling on the trichoscopy.

This result was consistent with the clinical cases published by Jha et al. [49] in which a patient with LPP showed significant hair thickening after four sessions of injection of PRP 3 weeks apart. PRP was effective in at least improving hair thickening; another patient with LPP [50] performed four sessions of PRP (3 weeks apart) associated with topically administered minoxidil 2%. The authors also found significant hair thickening and that PRP could be used as an adjunctive treatment in improving hair thickening when used along with topically administered minoxidil.

Frontal fibrosing alopecia (FFA) is currently the most frequent cicatricial type of alopecia. It is a lymphocytic scarring alopecia characterized by progressive recession of the frontal and

temporoparietal hairline. The eyebrows, eyelashes, and body hair can be affected [51, 52].

The prevalence of FFA is currently increasing progressively. Treatments available are mainly used to stop the progression of the disease and to maintain the stabilization of the disease. Currently the most frequent treatments include orally administered finasteride and dutasteride, topical/intralesional/systemic steroids, topically administered minoxidil, topically administered tacrolimus, and orally administered hydroxychloroquine [53–56].

Özcan et al. [57] reported a clinical case of a patient diagnosed with FFA and 4 cm recession of the frontotemporal hairline, perifollicular erythema, scaling, and lichenoid papules on the frontal and temporal scalp. After failure of several conventional treatments and as a result of further recession of the frontotemporal hairline, absence of hair regrowth on the eyebrows, and persistence of clinical signs, the use of PRP was considered. The authors performed five sessions with PRP injected into the frontotemporal hairline and eyebrows of the patient. After 1 month, the authors reported an improvement of perifollicular erythema, scaling, and lichenoid papules on the frontotemporal hairline. No further hair loss was noted after 5 months.

The reason why PRP might be useful in cicatricial alopecia is unknown. One of the hypotheses could be that various GFs would help diminish the inflammation, protecting and stimulating the new follicle. Cicatricial alopecia involves inflammation directed at the upper part of the hair follicle, where the stem cells and sebaceous gland reside [48]. In addition, anti-inflammatory, proangiogenic cytokines such as TGFβ and TGFβ1 are present in PRP platelet granules and may contribute to the effectiveness of PRP in PCAs [47].

CONCLUSIONS

On the basis of the published literature and considering that PRP may act at the dermal papilla cells to promote new hair growth, contribute to faster telogen–anagen transition, and increase hair density, good results should be expected with the use of PRP.

In androgenetic alopecia, a positive effect was demonstrated after injections of PRP (mainly after three treatments), showing an increase of hair density in most patients. PRP treatment can be administered alone or in combination with other therapies for AGA, although better results are obtained if PRP administration is used in association with topical (such as minoxidil) or oral therapies (finasteride).

Regarding its use in alopecia areata, the results obtained with the use of PRP are not so consistent. It some types of AA, PRP could be a valid treatment option to consider but not for all, such as AA totalis, in which no regrowth was noted.

Recently, it has been postulated that PRP might work in some types of cicatricial alopecia, such as lichen planopilaris and frontal fibrosing alopecia, although more clinical trials are needed to generate further evidence.

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