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Review of the Use of Platelet-Rich Plasma in the Treatment of Alopecia

Emma Coleman, RGN

Platelet-rich plasma (PRP) therapy is a new approach in dermatology and there is evidence to suggest that it provides excellent adjuvant treatment for nonscarring alopecia cases. There is evidence supporting the hypothesis that PRP therapy increases hair growth and thickness in patients with nonscarring alopecia. Studies including participants with scarring alopecia are limited and larger scale studies with tighter controls in PRP preparation, administration, and follow-up are needed to determine whether this is a clinically sound approach. Further symptom control analysis is also warranted as in both single and combination PRP therapy trials there are little data to support treatment effect on symptoms such as burning and itching. In this article, the author explains PRP preparation processes and PRP types and compares stand-alone PRP therapy with combination PRP study results. The author also makes recommendations for treatment and discusses the future of PRP research.

Platelet-rich plasma (PRP) therapy is a new approach in dermatology and there is evidence to suggest that it provides excellent adjuvant treatment for nonscarring alopecia cases (Garg & Manchanda, 2017; Saxena, Saxena, & Savant, 2016). Traditionally, minoxidil, finasteride, and steroids have been used for treatment of nonscarring and scarring alopecia. Platelet-rich plasma is not recognized by the National Institute for Health and Care Excellence (2018) as a treatment for alopecia. The efficacy of PRP in hair regrowth and condition is controversial as there is variation in trial execution, results are often measured by subjective questionnaires, and the sample sizes are small. Even marginally varying PRP preparation methods result in differing solution concentrations (Kaur & Kumaran, 2014; Table 1). This suggests a need for standardized preparation protocols and large-scale, double-blind placebo studies with objective results analysis (Cavallo et al., 2016; Garg & Manchanda, 2017).

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In this article, the author explains PRP preparation processes and PRP types and compares stand-alone PRP therapy with combination PRP study results. The author also makes recommendations for treatment and discusses the future of PRP research.

DISCUSSION

According to Garg and Manchanda (2017), PRP exhibits "molecular locking" of ectodermal and mesenchymal components for survival and integrity of hair follicles. It boosts keratinocyte, dermal papilla, and nerve cell and vasculature activity, promoting fibroblasts and growth factors (GF). It is possible that PRP exerts an anti-inflammatory effect by suppressing cytokine release. Patients with scarring alopecia generally respond poorly to grafting and adjuvant therapies due to irreversible follicular damage, whereas nonscarring forms of alopecia have higher success rates as they are self-limiting. This highlights the importance of differentiation and further study for best clinical outcome.

PRP Preparation Process

- **Extraction:** Whole blood is taken from the patient and placed into a machine designed to separate platelets from other blood components. There are a variety of extraction and centrifuge systems on the market with different mechanisms for accomplishing this (Cavallo et al., 2016; Garg & Manchanda, 2017).
- **Activation:** Calcium chloride and/or thrombin solution is added to the platelets to activate the solution by
  - degranulating platelets to release growth factors (GF) *or*
  - clotting platelets to create a gel that allows for precise application.

Some physicians avoid activation, preferring to inject platelets in their pure form and relying on patients' bodies to activate the cells naturally. Direct activation in situ should never be attempted (Cavallo et al., 2016).

- **Application:** Platelets actively secrete GF within 10 min after activation with more than 95% of GF secreted within 1 hr, making it essential to use

extracted platelets without delay (Garg & Manchanda, 2017). If prepared using sterile technique, the platelets remain viable and sterile for up to 8 hr (Marx, 2004). Methods of PRP scalp application include nappage (i.e., superficial injections) and dermaroller (i.e., microneedling), sometimes combined with massage (Cervantes et al., 2018). Optimum treatment is generally six sessions, 2 weeks apart. Results are observed at 4–12 weeks (Bajaj, 2019).

Common patient PRP application side effects include pain, eyelid swelling, headaches, seborrheic dermatitis, pruritis, infection, and development of scar tissue (Nall, 2017; Shah, Shah, Solanki, & Raval, 2017).

There is evidence to suggest that a double-spin method achieves greater platelet concentration than a single-spin method (Kurita et al., 2008). A platelet concentration of more than 1 million/μl is typically considered to be a therapeutically effective concentration of PRP (Kaur & Kumaran, 2014).

Cavallo et al. (2016) compared the way that using different activators affected GF stimulation post-PRP injection. The results of the study showed that a combination of thrombin with collagen I or calcium chloride promoted rapid GF release that remained stable for up to 24 hr, whereas calcium chloride alone stimulated a much lower initial release of GF that increased and reached higher levels at the 24-hr mark. The researchers stated that there is a lack of research into the benefits of leucocyte-rich versus leucocyte-free PRP preparations. Platelet-rich plasma variations are shown in Table 1.

Single PRP Therapy Research

Table 2 summarizes several PRP therapy clinical trials that included participants with both nonscarring and scarring alopecia. From these data, the following observations can be made:

- The mean number of participants included in trials studying nonscarring alopecia is 20. The mean number of participants included in trials studying scarring alopecia is 2.
- Most of the trials used the double-spin method. In those studies, the mean percentage of reduction in hair loss was 85%, versus 68% in the single-spin studies. These studies included participants with both scarring and nonscarring alopecia.
- Most studies used a calcium-based activator and at least two did not use an activator. These results demonstrate that there is no obvious correlation between success rates and use of an activator.
- Three of the studies showed hair quality improvement (Gkini, Kouskoukis, Tripsianis, Rigopoulos, & Kouskoukis, 2014; Gupta, Revathi, Sacchidanand, & Nataraj, 2017; Puig, Reese, & Peters, 2016).

All studies showed that PRP was successful with a mean success rate of 70% in the studies of patients with nonscarring alopecia and a success rate of 100% in the studies of the very small groups of patients with scarring alopecia. The success of using PRP combined with hair transplant in patients with lichen planopilaris seems promising and is attributed to the actions of insulin-like GF, basic fibroblast GF, and vascular endothelial GF found in abundance in PRP, which improve hair follicle perfusion (Saxena et al., 2016).

This analysis does not cover all trials; however, the data collected suggest that PRP is a viable therapy option for treatment of nonscarring forms of alopecia and also show promise for the treatment of scarring alopecia, although there is a lack of objective results analysis, uniform preparation protocols, and large-scale studies, particularly with patients with scarring alopecia. Trichoscopy

TABLE 1. Classification of Platelet Concentrates

Type of PRP	Description
Pure platelet-rich plasma (P-PRP)	Prepared with slow-spin centrifugation. Only the superficial "buffy" coat layer is extracted and prepared for the second centrifuge cycle. Results in a high concentration of platelets but most leucocytes are not collected.
Leucocyte and platelet-rich plasma (L-PRP)	Following the initial centrifuge, the platelet and plasma solution and entire "buffy" coat layer, plus 1–2 mm of red blood cells are removed. The second spin is then carried out. Results in a fibrin-rich plasma with a high platelet and leucocyte concentration, plus suspension of red blood cells.
Pure platelet-rich fibrin/matrix (P-PRF/M)	This is created when P-PRP is mixed with an activator and allowed to incubate for some time, after which a stable PRF/M clot can be collected. Contains a low concentration of leucocytes.
Leucocyte and platelet-rich fibrin (L-PRF)	The blood is immediately centrifuged without being treated with an anticoagulant. Natural coagulation occurs where three layers form, a(n) • red blood cell base layer, • L-PRF clot in the middle, and • acellular plasma layer at the top. This encourages platelets and leucocyte growth factors into the fibrin matrix. The clot can be prepared and used as part of the therapy.

Note. From Kaur and Kumaran (2014).

TABLE 2 Platelet-Rich Plasma Clinical Trials

First Author (Year)	Alopecia	Sample Size	Mode of Preparation Activator	Follow-up	Results
Anitua et al. (2017)	Nonscarring	19	Single-spin Calcium chloride and anticoagulant[a]	1 year using questionnaire	79% of participants reported significant decrease in hair loss
Gkini et al. (2014)	Nonscarring	22	Single-spin Calcium gluconate (1:9 ratio)	1 year using questionnaire	85% of participants reported improvement in hair quality and texture 65% of participants reported increased hair density
Gupta et al. (2017)	Nonscarring	30	Double-spin No activator reported	6 months using questionnaire	93% of participants reported complete cessation of hair loss after 2 months 68% of participants reported increase in hair growth 37% of participants reported improved hair texture
Khatu et al. (2014)	Nonscarring	11	Double-spin Calcium chloride (1:9 ratio)	12 weeks using questionnaire	70% of participants reported improvement
Puig et al. (2016)	Nonscarring	26	Double-spin[b]	Not reported	13.3% of participants in the treatment group reported reduction in hair loss 26.7% of participants in the treatment group reported thicker heavier hair than 18% of participants in the control group
Trink et al. (2013)	Nonscarring	45	Single-cycle (8 min) Calcium gluconate	10 months 1 year	Significant increase in hair regrowth Reduced hair dystrophy Reduced burning and itching 35%–40% of participants reported spontaneous disease remission
el-Fakahany, Raouf, and Medhat (2016)	Nonscarring and scarring	3	Not stated	Every 28 days until 6 months	100% of participants were satisfied
Saxena et al. (2016)	Scarring (lichen planopilaris)	1	Double-spin Acid citrate[c] with hair transplant	10 months	80% success rate of hair transplant

[a]Endoret (BTI Technology Institute, Blue Bell, PA).
[b]Angel System (Arthrex, Inc., Naples, FL).
[c]Remi 4RC (REMI, Amhearst, MA).

would provide a more reliable form of evaluation (Khatu, More, Gokhale, Chavhan, & Bendsure, 2014).

Combination PRP Therapy Research

Table 3 summarizes several combination PRP therapy clinical trials that included patients with nonscarring alopecia. From these data, the following observations can be made:

- All studies included participants with nonscarring alopecia.
- The mean number of participants across these studies is 36.
- Several of the study participants had previously experienced unsuccessful treatment with minoxidil or finasteride (Lee et al., 2015; Mubki, 2016).
- Although difficult to ascertain, the mean hair improvement seen among the combination groups is approximately 60.25%.
- There was no significant difference in the study results based on whether a single-spin or double-spin process was used.
- There is evidence to suggest that combination therapy increases hair thickness (Lee et al., 2015).
- Conversely, research has suggested that using PRP in combination with topical minoxidil has a cumulative effect on dermal papilla cells, promoting angiogenesis resulting in an improvement in hair regrowth, superior hair count, anagen/telogen ratio, and patient satisfaction at 6 months (Anitua, Pino, Martinez, Orive, & Berridi, 2017).
- In all cases, clinical and quantitative evaluation tools were used to pinpoint results.
- The biological activators and follow-up times among the studies vary, making it difficult to draw objective conclusions about successful combination therapy.

TABLE 3 Platelet-Rich Plasma Clinical Trials Using Combination Therapy

First Author (Year)	Alopecia	Sample Size	Mode of Preparation Activator	Follow-up	Results
Lee et al. (2015)	Nonscarring	40	Double-spin Polydeoxyribonucleotide and PRP	12 weeks	Polydeoxyribonucleotide and PRP showed a significant improvement in hair thickness compared with polydeoxyribonucleotide without PRP ($p = .031$)
Mubki (2016)	Nonscarring	1	Not stated Right head: Intralesional triamcinolone acetonide and intradermal PRP Left head: Intradermal PRP	16 weeks	Digital photography and trichoscopy showed less than 25% overall improvement, but the combination-treated side showed slightly greater improvement
Schiavone, Raskovinc, Greco, and Damiano (2014)	Nonscarring	64	Single-spin at baseline Double-spin at 3 months L-PRP and concentrated plasmatic proteins	12 weeks	97% of participants reported a significantly important difference in hair growth using macrophotography and the Jaescheke Rating of Clinical Change Scale
Shah et al. (2017)	Nonscarring	50	Not stated Topical minoxidil and PRP compared with PRP	6 months	24% of participants in the combination therapy group and 4% of participants in the monotherapy group had excellent improvement in hair growth and condition
Takikawa et al. (2011)	Nonscarring	26	Double-spin Sodium chloride/Dalteparin and protamine microparticles	12 weeks	Trichoscopy showed thickened epithelium, proliferation of collagen fibers and fibroblasts, and increased blood vessels around hair follicles.

Note. L-PRP = Leucocyte and platelet-rich plasma; PRP = Platelet-rich plasma.

- All studies show that PRP is effective in creating optimum hair growth conditions and/or improving physical hair condition.

CONCLUSION

Platelet-rich plasma therapy increases hair growth and thickness in patients with nonscarring alopecia. Research including participants with scarring alopecia is limited, and larger scale studies with tighter controls in PRP preparation, administration, and follow-up are required to determine whether this is a clinically sound approach. Further symptom control analysis is also warranted as in both single and combination PRP therapy trials there are little data to support treatment effect on symptoms such as burning and itching.

Analysis of combination versus stand-alone PRP therapy shows that isolated PRP trials had fewer participants and a higher success rate (70%) than the success rate for combination therapy (60.25%) in patients with nonscarring alopecia, although access to precise data was limited. The double-spin method yields superior results.

Recent studies have researched use of epidermal cells and dermal papilla cells in combination with PRP to promote hair growth on the skin of nude mice. Hair was shown to grow at a faster and thicker rate due to PRP-induced versican and β-catenin stimulation, (Miao et al., 2013; Xiao, Miao, & Wang, 2017). Another recent study demonstrated PRP's effect on stem cell survival and cutaneous tissue regeneration. The researchers found that wounds treated with PRP showed a faster healing rate due to enhanced morphogen communication, which triggered tissue development, increased Rouget cell recruitment, and blood vessel formation, (Bhang, Park, Yang, Shin, & Kim, 2013).

A current American trial including 60 participants with a diagnosis of alopecia areata or scarring alopecia aims to directly compare scalp treatment using PRP with adipose-derived tissue stromal vascular fraction and to analyze the results using trichoscopy and photographic evidence. The relevant data collection will be completed during the first quarter of 2019 (The Belgravia Centre, 2019).

Imminent future research with nonscarring alopecias will include studies investigating the use of Janus kinase inhibitors, which may help speed up the hair growth cycle. Gut microbiome and wider PRP studies are also expected (Alopecia, 2018).

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