Platelet-Rich Plasma for the Treatment of Androgenic Alopecia: A Systematic Review

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Abstract

The use of platelet-rich plasma (PRP) has become increasingly commonplace in facial plastic surgery for the treatment of androgenic alopecia (AGA). However, this treatment remains novel with a range of application techniques and outcomes described in the literature. Herein, the authors systematically review the existing literature on the use and efficacy of PRP for AGA. Systematic review of PubMed, Embase, and Cochrane databases was performed. Case reports were excluded. Twenty-four papers met inclusion criteria for this study: 8 randomized control trials and 16 prospective cohort studies. Twenty-one studies used clinical criteria to diagnose AGA, while three used confirmatory biopsies. PRP was injected with or without the use of a numbing agent, and most studies performed multiple injections (three or more separated by several weeks). Twenty-one studies reported positive outcomes by objective criteria (88%), while three suggested that there was no clinical improvement, although in two of these studies patients still reported increased satisfaction. There were no complications reported other than transient edema/erythema and pain/headache associated with the procedure. The existing literature suggests that PRP is a low-risk intervention to treat AGA associated with good patient satisfaction and objective improvements in outcomes. Further research is needed to optimize preparation and delivery methods as well as standardize measurements of clinical outcomes.

Keywords
- hair loss
- hair density
- growth factors
- platelet rich plasma
- androgenic alopecia

Androgenetic or androgenic alopecia (AGA) is a disease of progressive hair loss mediated by systemic androgens and other genetic factors. It is the most common type of hair loss across both genders. Estimates of the prevalence of AGA vary, but AGA affects >73% of men and >57% of women by the age of 80 years.[1,2] As much as 58% of the male population between 30 and 50 years of age have AGA.[3] AGA can lead to significant negative psychosocial effects,[4] and improvement in hair loss has been shown to improve layperson perception of age, attractiveness, successfulness, and approachability.[5]

There is a wide range of clinical treatments for hair loss, including the Food and Drug Administration (FDA)-approved medical treatments of topical minoxidil, oral finasteride, and low-level laser light therapy. Surgical options include follicular unit transplant and follicular unit extraction techniques, which are outpatient procedures with excellent reported outcomes.[6,7] In addition to these existing medical and surgical options, platelet-rich plasma (PRP) is a new minimally invasive, office-based procedure used to treat hair loss secondary to androgenic causes. PRP contains growth factors extracted from autologous blood after venipuncture. PRP has been used since the early 2000s across medical fields, including ophthalmology, orthopaedics, and cardiac surgery. While PRP preparation systems are regulated by the FDA, PRP as a blood product is exempt from the FDA's traditional regulatory pathway.[8] Nearly all preparation systems were designed to generate PRP to be mixed with bone graft material for orthopaedic applications. All other uses of PRP are currently considered off-label applications.

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Uses for PRP in the field of facial plastic and reconstructive surgery include soft tissue augmentation,[9] skin rejuvenation,[10,11] and wound healing.[12,13] A recent review by Sand et al in 2017 examined the early body of evidence for PRP in areas of aesthetics, including hair loss and facial rejuvenation. Although it was not a formal systematic review, the article examined 14 recent studies on PRP treatment for AGA and suggested promising outcomes. However, the review highlighted the need for a formal systematic review, because of the variance in how the limited studies varied widely in the procedures conducted and outcomes measured. Herein, we perform an up-to-date systematic review of the literature to examine patient demographics, PRP delivery procedures, and subjective and objective outcomes including third-party assessments, patient satisfaction surveys, hair count, and hair density.

Methods

Search Strategy

A systematic review was performed targeting studies investigating the use of PRP for the treatment of AGA. In October 2017, a literature search was conducted using PubMed, Cochrane, and Embase using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations (►**Fig. 1**).[14] For PubMed, the initial search included articles that mapped to the medical subject headings "platelet-rich plasma," or the text word "platelet-rich" was collected into a first group. Next, those that mapped to the medical subject heading "alopecia" or text word "hair" were collected into a second group. These two groups were cross-referenced and limited to those with human subjects and written in the English language. Search terms used were: "Platelet-Rich

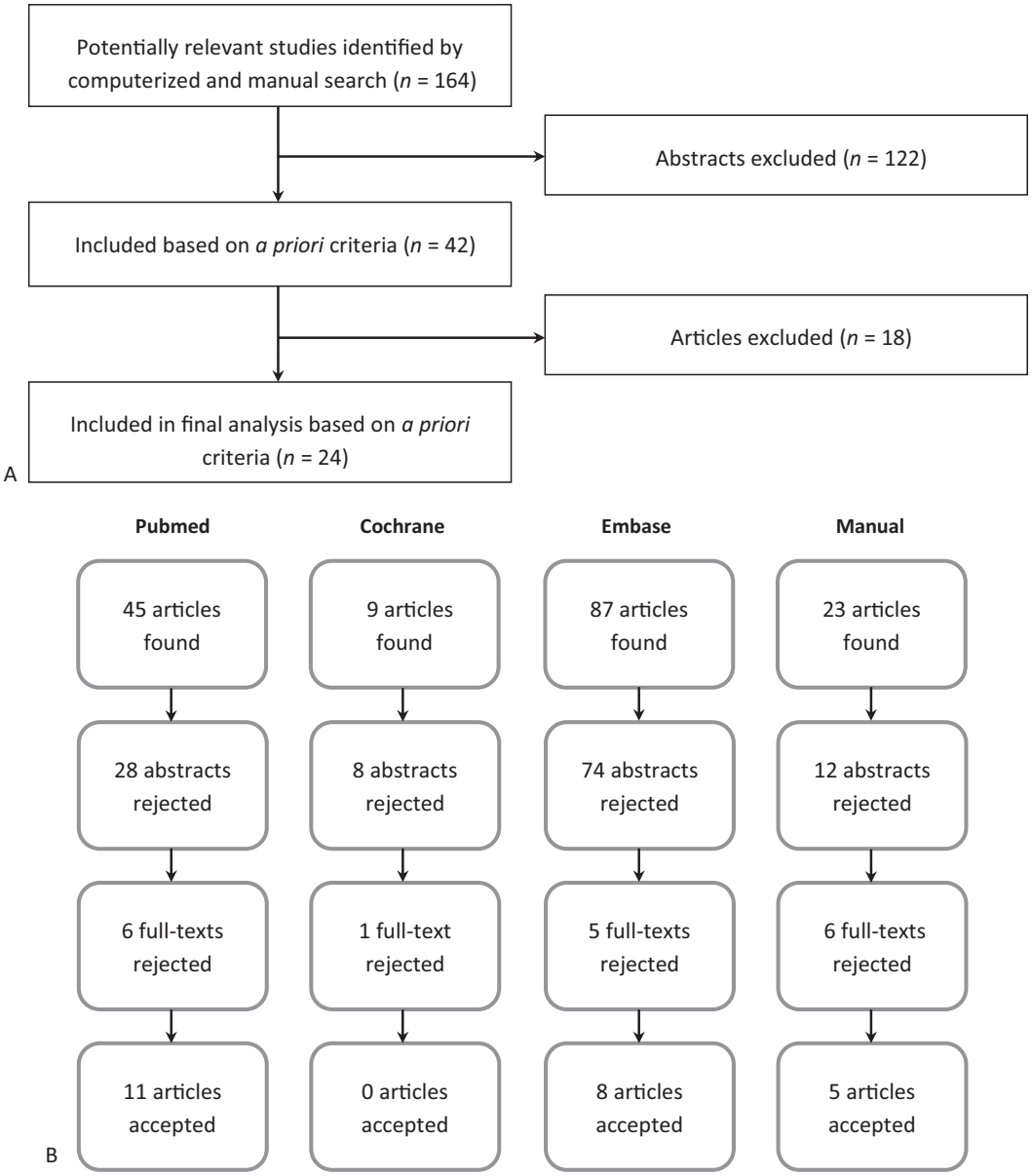

Fig. 1 Flowcharts of selection process for papers included in this systematic review, conducted per PRISMA guidelines. (**A**) Stages of identification of studies and (**B**) stages of identification by citation source.

Plasma" [Mesh] OR "platelet-rich" [tw] AND "Alopecia" [Mesh] OR "Hair" [tw] AND "Humans" [Mesh] AND English [lang].

Titles and abstracts were screened to identify relevant studies, for which full texts were accessed and reviewed against predetermined inclusion and exclusion criteria (see below). Independent searches were performed by two individuals. The initial computerized search yielded 45 studies of which 11 met the inclusion criteria for this study.

The Cochrane Database of Systematic Reviews was searched for articles with the text words "hair loss" and "platelet," revealing nine articles, none of which met the inclusion criteria for this study. Embase was also similarly searched for studies with the Emtree-exploded term "thrombocyte-rich plasma" and was mapped with those that have the Emtree-exploded terms "alopecia" or "hair loss." This search yielded 87 citations in the English language, which were screened by titles, abstracts, and full texts, from which 8 new articles were found. Manual review of bibliographies of accepted papers revealed five additional papers that met inclusion criteria.

Variables and Inclusion/Exclusion Criteria

Inclusion and exclusion criteria were designed to capture as many studies as possible for review, and no papers were excluded on the basis of quality. Articles identified by the computerized and manual searches were subject to the following inclusion criteria: (1) subjects had hair loss due to AGA, and (2) PRP was administered to treat hair loss. Articles were excluded if they were (1) case reports or case series or (2) if the patients undergoing PRP treatment had recent or concurrent medical or surgical therapies for hair loss including hair transplantation, using Rogaine (minoxidil) or Propecia (finasteride).

Study Analysis

Variables assessed included overall efficacy of therapy (as reported through patient satisfaction, objective measurements, and third-party evaluations), the efficacy in men compared with women, the number of treatments used, side effects/complications of treatment, procedures for delivering PRP, and complications. Accepted articles were assessed for patient demographics, study design, sample size, outcome measures, and conclusions. Heterogeneity among studies measuring the same outcomes was evaluated using the I^2 statistic (a measure of variation that exists between studies that exceeds that created by random chance). Relatively homogenous study populations have an I^2 value of 0 to 60%, while larger I^2 statistics suggest substantial heterogeneity among studies not amenable to meta-analysis. Where the I^2 statistic was $< 60\%$, data were formally pooled into a meta-analysis. Calculations were made using MedCalc (MedCalc Software) and Microsoft Excel (Microsoft Corp.).

Results

Titles and abstracts for all identified studies were reviewed, and ultimately, 24 studies were included in the systematic review (►**Fig. 1**). Eight studies were randomized clinical trials (RCTs),[7–14] and 16 were prospective cohort studies.[12,15–29]

Patient Demographics

A total of 471 patients were studied, of which 131 (28%) were female (►**Table 1**). The mean age of the patients in included studies ranged from 29.6 to 43 years of age, although many studies reported only a range of ages. Other patient demographics such as race and hair color were not included in enough studies to merit reporting. Most studies excluded patients according to preset exclusion criteria that most commonly included (1) use of topical or oral medication within a certain time period of study initiation (e.g., 60 days or 12 months), (2) history of bleeding disorders or recent use of aspirin or nonsteroidal anti-inflammatory medication, (3) history of keloids, and (4) history of immunosuppression or systemic disease, such as human immunodeficiency virus (HIV) or hepatitis. The vast majority of studies diagnosed AGA clinically, while three studies also used incisional punch biopsies to confirm the diagnosis.[30–32]

PRP Delivery Procedures

The delivery procedures of PRP in the different studies are outlined in ►**Table 2**. The delivery of PRP in the majority of studies was accomplished through injections using small gauge needles (e.g., 30-gauge, insulin syringes). Only two studies formulated PRP into a topical spray, although one used it as an adjunct to injections.[18,33] A local anesthetic numbing agent was used in at least eight studies and was otherwise not reported in many others. The area of scalp treated varied widely between studies, but the most common areas were the frontal, parietal, and occipital scalp. The majority of studies (14 of 24) used activated PRP, typically via treatment with calcium chloride. Most studies used more than one treatment of PRP per patient: 20 of 24 studies used between 3 and 6 treatments. Three was the most common number of treatments used per patient during the study period, most often with 1 month intervals between each injection.

Outcomes

The outcomes of applying PRP in patients with AGA are outlined in ►**Table 3**. The shortest follow-up time for studies was 6 weeks, and the longest was 1 year. Twenty-one (88%) of 24 studies reported positive outcomes. Thirteen studies (54%) reported statistically significant improvement in at least one objective outcome. Hair counts or hair densities were described by 16 studies,[15,17,20,21,23,24,26,28,30–37] and of these, 12 found statistically significant improvements in one of these objective outcomes.

Among studies with the highest level of evidence, six (75%) of eight RCTs reported positive treatment outcomes. All studies were half-head studies with PRP injections compared with saline injections, with the exception of one study by Farid et al that used a separate control group treated with minoxidil. Gentile et al performed a double-blinded RCT with 18 male patients and found that three sessions of non-activated PRP injections spaced 30 days apart increased hair count and density after 12 weeks as compared with controls.[30] Cervelli et al[36] and an older study by Gentile et al[32] found that three treatments of activated PRP given at 1-month intervals improved hair density count and hair

Table 1 Study demographics

Study	No. of patients (n, % female)	Age	Controls (*n*, half head?)	Exclusion criteria: A. Recent use of topical/ oral medications B. Bleeding disorders, anticoagulation C. Smokers D. Pregnant E. Scalp conditions other than AGA F. Propensity for keloids G. Immunosuppressed of systemic infections or untreated diabetes	Clinical or biopsy diagnosed AGA
Randomized controlled trial					
Gentile et al[30]	18, (0, 0%) for non-activated PRP 6 (0, 0%) for activated PRP	Mean 37.4 for non-activated PRP Mean 40.8 for activated PRP	Non-activated PRP: Placebo (18, half head) Activated PRP: no control	A, B, F, G, and advanced hair loss stage 5–7	Biopsy
Tawfik and Osman[34]	30 (30, 100%)	Mean 29.3	Placebo (30, half head)	A, B, D, F, G	Clinical
Alves et al[35]	22 (11, 50%)	Mean 39	Placebo (22, half head)	A, B, C, D, E or history of hair transplant	Clinical
Mapar et al[38]	19 (0, 0%)	Range 24–45	Placebo (19, half head)	B, E, G or recent aspirin use	Clinical
Puig et al[31]	26 (26, 100%)	Age 18+	Placebo (11)	A	Clinical or biopsy
Gentile et al[32]	23 (0, 0%)	Mean 35	Placebo (23, half head)	A, B, F, G	Biopsy
Farid et al[33]	20 (16, 80%)	Mean 29.6	Group treated with minoxidil lotion (20)	A, D, E, hyperandrogenemia	Clinical
Cervelli et al[36]	10 (0, 0%)	Mean 33	Placebo (10, half head)	A, F, G	Biopsy
Prospective cohort study					
Anitua et al[15]	19 (6, 32%)	Range 27–60, (mean 45 + /− 11)	–	A, E	Clinical
Jha et al[16]	20 (unknown, likely 0%)	Range 18–45	Group treated with minoxidil lotion and oral finasteride (20)	B, F, G, malignancy, HIV/HepB/HepC	Clinical
Kachhawa et al[17]	44 (0, 0%)	Mean 34 (18–55)	Placebo (44, half head)	A, B, G, patients with unrealistic expectations, current infection, malnutrition	Clinical
James et al[18]	5 (0, 0%)	Range 30–50	–	A, G	Clinical
James et al[19]	10 (2, 20%)	Range 30–50	–	A, G	Clinical
Rodrigues et al[20]	15 (0, 0%)	Range 18–50	–	B, G, recent ASA/NSAID use, or history of hair transplant	Clinical
Borhan et al[21]	14 (0, 0%)	Range 18–60	–	A	Clinical
Singhal et al[22]	10 (2, 20%)	Range 25–35	Placebo	A, B, D, E, F, G, uncooperative patients	Clinical
Gkini et al[23]	20 (2, 10%)	Mean: 34	–	A, B, E, F, G, anticoagulation	Clinical
Kang et al[12]	26 (11, 42%)	Mean 37.2	Group treated with interfollicular placental extract injections (13)	A, F, G	Clinical
Khatu et al[24]	11 (0, 0%)	Range 20–40	–	B, E, G	Clinical
Marwah et al[25]	10 (0, 0%)	Unknown	–	Not noted	Clinical
Sclafani[26]	15 (6, 20%)	Mean 43	–	Not noted	Clinical
Betsi et al[27]	42 (8, 19%)	Range 32–67	–	E, G	Clinical
Takikawa et al[28]	26 (10, 38%)	Range 28–59	Placebo (26, half head).	Not noted	Clinical
Greco et al[29]	10 (1, 10%)	Unknown	Placebo (5)	Not noted	Clinical

Abbreviation: PRP, platelet-rich plasma.

density at 3 months follow-up in 10 male patients and 23 male patients, respectively. Similarly, Alves and Grimalt[35] studied 22 patients given three injections of PRP or saline at 1-month intervals; after 6 months, a statistically significant improvement in hair density was identified in treated half-heads. Tawfik and Osman[34] studied 30 female patients given injections weekly for a maximum of four sessions; patients had been followed up for 6 months, and a statistical significant difference was noted between PRP and placebo-treated areas in both hair density and hair thickness.

Table 2 Study procedures

Study	Activated PRP?	Area of scalp treated	Delivery method	Total amount of agent used per treatment	No. of treatments, interval	Numbing agent
Randomized controlled trial						
Gentile et al[30]	Both non-activated and activated	Non-activated PRP: Scalp divided into frontal, parietal, vertex and occipital. If patient had frontal-parietal hair loss, PRP injected to the frontal scalp and placebo into the vertex. If the patient had parietal-vertex hair loss, PRP was injected into the parietal scalp and saline into the vertex. Activated PRP: 4 cm^2 frontal	Non-activated PRP: interfollicular injection with Ultim gun, 30 G needle Activated PRP: 25 G needle	Non-activated: 0.2 mL/cm^2 Activated: 0.25 mL/cm^2	Non-activated: 3, monthly Activated: 1	No
Tawfik and Osman[34]	Yes	Unknown	Insulin syringe	Unknown, <10 mL	4, weekly	Not noted
Alves et al[35]	Yes	Two circular areas (one frontal and one occipital) in both treatment and control half heads Four circular areas were defined and marked centrally with a red permanent tattoo.	30 G needle	3 mL	3, monthly	No
Mapar et al[38]	Yes	Two square-shaped areas of 2.5 cm × 2.5 cm, at least 3 cm apart from each other were selected on the scalp of each patient as case and control sites	30 G needle	1.5 mL	2, monthly	Not noted
Puig et al[31]	Yes	10 cm^2 area in central scalp	Subcutaneous injection	10 mL	1	Yes
Gentile et al[32]	No	Scalp divided into frontal, parietal, vertex and occipital. If patient had frontal-parietal hair loss, PRP injected to the frontal scalp and placebo into the vertex. If the patient had parietal-vertex hair loss, PRP was injected into the parietal scalp and saline into the vertex.	30 G needle	9 mL, injected 0.1 mL/cm^2	3, monthly	No
Farid et al[33]	No	Imaginary vertical lines along the affected areas of the scalp.	30 G needle injection, followed by manual dermaroller (0.5-mm needles), the remaining sprayed over the area and dermarolled again	1 mL injected, 1 mL sprayed	6, monthly	Not noted
Cervelli et al[36]	Yes	If patient had hair loss in frontal and parietal region: PRP in frontal area and placebo in parietal If patients had hair loss in parietal and vertex regions, PRP in parietal and placebo in vertex	Injection	9 mL	3, monthly	No
Prospective cohort study						
Anitua et al[15]	Yes	Unspecified affected areas	30 G needle	3–4 cm^3	5, 3 monthly then months 4 and 7	Not noted
Jha et al[16]	No	Unspecified affected areas	Injection with insulin syringe followed by microneedling	Unknown	3, 3 weeks	Yes
Kachhawa et al[17]	No	Unspecified affected areas on the left side	Insulin syringe	1–2cc	6, 3 weeks	Yes
James et al[18]	Yes	Unspecified affected areas	Insulin syringe	Linear pattern 1-cm apart	Every 2–3 weeks for 3 months	Not noted
James et al[19]	Not noted	Unspecified affected areas	Twice a day spray	Unknown	6, twice monthly	No
Rodrigues et al[20]	Yes	Unspecified affected areas	20 subcutaneous injections of 100μL	Unknown	4, 15 days	Not noted
Borhan et al[21]	No	Vertex	32 G needle, 0.05–0.1 mL per injection	4–5 mL	4, 3 weeks between first three injections and 6 weeks for last injection	Not noted

(*Continued*)

Table 2 (*Continued*)

Study	Activated PRP?	Area of scalp treated	Delivery method	Total amount of agent used per treatment	No. of treatments, interval	Numbing agent
Singhal et al[22]	Yes	Unspecified affected areas	Insulin syringe	8–12 mL	4, 2 weeks	Not noted
Gkini et al[23]	Yes	Unspecified affected areas (frontal, parietal, occipital)	27 G needle in linear pattern at depth of 1.5–2.5 mm	~6 mL	3, 3 week intervals then 6 month booster	Yes
Kang et al[14]	Yes	Frontal and Parietal areas	Injection	4 mL, 0.05–0.1 mL/cm^2.	2, 3 months	Yes
Khatu et al[24]	Yes	1 cm × 1 cm area over right parietal area in mid-pupillary line	Multiple small injections in a linear pattern 1 cm apart with insulin syringe	2–3cc	4, 2 weeks	Yes
Marwah et al[25]	Not noted	Unspecified affected areas	Not noted	Not noted	6, weekly	Not noted
Sclafani et al[26]	Yes	2 cm 2 cm square in the midline	0.1ml injections intradermally separated by 5–8 mm.	8–9 mL	3, monthly	Not noted
Betsi et al[27]	Not noted	Unspecified affected areas	32 or 30.5 G needle	8–12 mL	5, all within 2 months	Yes
Takikawa et al[28]	Not noted	Frontal or Parietal sites with lanugo-like hair	25 G needle	3 mL	5, at weeks 0, 2, 4, 6, and 9	Not noted
Greco et al[29]	Not noted	Unspecified affected areas	1-mm microneedling roller, then PRP injections every centimeter, then PRP spray	10 mL	1	Yes

Abbreviations: G, gauge; PRP, platelet-rich plasma.

Three studies did not report positive findings after PRP administration including two RCTs. Mapar et al[38] performed a single-blinded trial of 19 male patients, finding that two injections of PRP administered 1 month apart did not increase the number of terminal and vellus hair after 3 or 6 months. In a double-blinded study of 26 female patients, Puig et al[31] reported no difference in hair counts 26 weeks after a single PRP treatment between treatment and placebo groups. However, subjectively, 26.7% of treated patients reported that their hair was coarser or heavier compared with 18.2% of control patients. Lastly, Marwah et al[25] performed a prospective cohort study administering six PRP treatments on 10 patients, finding clinical improvement by photography in only two (20%) patients. However, all patients were satisfied with their treatments.

Meta-analysis

Meta-analysis of data was limited by the variety in treatment procedures and outcomes reported by studies. Among the studies with the highest level of data—the eight randomized control trials—four reported a common outcome of hair density at 3 months. However, one study (Gentile et al[30]) used non-activated PRP so it was removed from this subgroup. The remaining three studies had an I^2 statistic of 74% for difference in treatment group hair density compared with difference in control group hair density over 3 months, suggesting significant heterogeneity among studies. Therefore, no meta-analysis was performed.

Complications

Few studies noted any complications from PRP treatment. Most noted temporary pain during injections[33,34] and transient edema/erythema at the injection site.[15,24] No allergic reactions, hematomas, or infections were reported.

Discussion

Twenty-four studies were included in this systematic review of PRP for AGA. Eight studies were randomized controlled trials, and 16 were prospective cohort studies. Of these 24 articles, 21 reported objectively positive results, suggesting that PRP is a promising new treatment for AGA. The treatment was tolerated well with minimal to no side effects reported. Of the three studies that reported no significant outcomes for the use of PRP in patients with AGA, two notably used fewer injections than the average study reviewed. Puig et al[31] and Mapar et al[38] used one and two treatments per patient, respectively, whereas the vast majority of studies used three or more injections administered monthly.

A meta-analysis was unable to be performed due to significant heterogeneity among the small number of studies that reported the same outcomes. The most consistently reported outcome across studies was hair density after 3 months of treatment, which was used by Gupta and Carviel[39] in their recent meta-analysis of three of the studies included in this systematic review. At the time of that publication, several RCTs had not yet been published, and Gupta et al were able to include only comparisons of treatment versus baseline analyses, finding

Table 3 Study outcomes

Study	Follow-up time	Positive interpretation of results?	One statistically positive outcome?	Objective outcome measures	Blinded or independent subjective assessment	Patient satisfaction surveys	Complications
Randomized controlled trial							
Gentile et al[30]	Non-activated: 12 weeks Activated: 6 months	Yes	Yes	Non-activated: Hair count,[a] hair density[a] Activated: hair density, follicular unit density (significant for one prep kit but not another)	–	–	–
Tawfik and Osman[34]	6 months	Yes	Yes	Hair density,[a] hair thickness[a], hair pull	–	Yes (mean overall satisfaction 7.0 out of 10)	Temporary pain and pinpoint bleeding at injection sites.
Alves et al[35]	6 months	Yes	Yes	Hair count, hair density,[a] anagen hair, Telogen hair, anagen/Telogen ratio, terminal hair density	–	–	Local injection pain
Mapar et al[38]	6 months	No	No	Terminal and vellus hair	–	–	–
Puig et al[31]	26 weeks	No	No	Hair count, "hair mass index"	–	Yes (13.3% vs 0% placebo reported improvement in hair loss, rate of hair loss, hair thickness, and ease of managing/styling hair)	–
Gentile et al[32]	12 months	Yes	Yes	Hair count,[a] hair density,[a] terminal hair density,[a] # of hair follicles,[a] epidermis thickness[a] # of small blood vessels around follicles,[a] # of Ki67+ basal keratinocytes,[a] vellus hair density	–	–	–
Farid et al[33]	28 weeks	Yes	Yes	Hair count[a]	Yes, 45% of patients had improvement	Yes (50 + /− 19.75 on a visual analog scale for improvement from 0 to 100)	Pain during injection
Cervelli et al[36]	12 months	Yes	Yes	Hair count,[a] hair density,[a] terminal hair density,[a] of hair follicles,[a] epidermis thickness,[a] # of small blood vessels around follicles,[a] # of Ki67+ basal keratinocytes,[a] vellus hair density	–	–	–
Prospective cohort study							
Anitua et al[15]	12 months	Yes	Yes	Hair density,[a] mean hair diameter,[a] terminal/vellus-like hair ratio,[a] hair shaft thickness among terminal follicles[a]	–	Yes (48% satisfied/very satisfied)	Transient erythema, local edema that disappeared after 24 hours.
Jha et al[16]	3 months	Yes	No[b]	Vellus and total hair, hair shaft diameter, reduction in yellow dots	–	Yes (satisfaction was at least 75% on a 0 to 100 scale for 90% of patients)	Mild pain in 7 patients, which subsided on the next day.
Kachhawa et al[17]	18 weeks	Yes	Yes	Hair thickness,[a] hair density,[a] hair pull	–	Yes (70% reported increased hair quality/ thickness, 55% reported increased hair density)	Pain that subsided after 4 hours.

(*Continued*)

Table 3 (*Continued*)

Study	Follow-up time	Positive interpretation of results?	One statistically positive outcome?	Objective outcome measures	Blinded or independent subjective assessment	Patient satisfaction surveys	Complications
James et al[18]	3 months	Yes	No[b]	None	–	–	–
James et al[19]	3 months	Yes	No[b]	None	–	–	–
Rodrigues et al[20]	150 days	Yes	Yes	Hair count,[a] anagen hair[a]	–	–	–
Borhan et al[21]	4 weeks	Yes	No[b]	Percent hair gain, hair density	Yes, equivocal among three evaluators (2 independent)	Yes (100% noted improvement in texture, 50% noted growth back, etc.)	–
Singhal et al[22]	12 weeks	Yes	No[b]	Hair pull test	–	–	Mild headache ($n = 3$) alleviated by paracetamol.
Gkini et al[23]	12 months	Yes	Yes	Hair density[a]	–	Yes (mean rating of 7.1 on a scale of 1–10).	Mild pain (100%), scalp sensitivity (60%) during first hair wash
Kang et al[12]	6 months	Yes	Yes	Hair count,[a] hair thickness,[a] "two-point scoring method"[a]	–	–	Transient erythema/ edema
Khatu et al[24]	3 months	Yes	No[b]	Hair count, hair pull test	–	Yes (mean rating of 7.0 on a scale of 1–10).	Minimal pain, redness and pinpoint bleeding.
Marwah et al[25]	6 weeks	Equivocal	No[b]	None	–	Yes ("all patients were satisfied with the results")	–
Sclafani et al[26]	6 months	Yes	Yes	"Hair density index"[a]	–	Yes (not systematically reported)	Mild-moderate pain during treatment.
Betsi et al[27]	3 months	Yes	No[b]	Hair pull test	–	Yes (mean rating of 7.0 on a scale of 1–10)	Drowsiness and sensible scalp (31%).
Takikawa et al[28]	12 weeks	Yes	Yes	Hair count, hair cross-sectional thickness[a]	–	–	Temporary pain at the injection site
Greco et al[29]	8 months	Yes	No[b]	Hair shaft diameter	–	–	–

[a]Statistically significant.
[b]No statistical tests performed in this study.

I^2 statistic of 0% (low heterogeneity of data) and ultimately a standardized mean difference of 0.51 (interpreted as a moderate effect size). Notably the analysis included one RCT,[36] but comparison to controls was not possible as remaining studies were cohort studies.[21,23,28] In this updated systematic review, the advantage of including several new studies with a high level of evidence did not translate into a usable meta-analysis statistic.

The limitations of this systematic review are found primarily in the quality of the included studies and the consistency of methods between studies. The 24 articles included in this analysis varied greatly in quality, ranging from brief reports of small patient populations and unclear methods to large double-blinded placebo-controlled half-head trials of up to 30 patients with detailed inclusion and exclusion criteria and well-defined outcomes. Quantitatively, studies varied dramatically in patient enrollment, sex of patients enrolled, and the quality of measured outcomes. Exclusion criteria varied greatly between studies, most notably as related to the how recently patients could use the FDA-approved medications for hair loss (finasteride and minoxidil). There were also several studies that allowed patients to use oral medications during the duration of the study that had to be excluded based on the *a priori* exclusion and inclusion criteria of this systematic review, to make the data and outcomes more clear for interpretation. For example, Schiavone et al studied 64 consecutive patients treated with a single injection of PRP, and two independent evaluators rated improvement in macrophotographs for over 95% of patients after 6 months; this study could not be included in this systematic review, however, as some patients who were using minoxidil or finasteride were encouraged to continue using their medications.[40]

Treatments with PRP were not uniform across studies. Most studies describe using 10 to 20 mL of blood from a peripheral venipuncture to produce 2 to 5 mL of PRP product using a variety of preparation kits. This was typically injected with a small gauge needle. James et al[18] notably did not inject PRP, but instead used it in a topical spray product. Farid and Abdelmaksoud[33] also employed a spray in addition to injections. Some studies used activated PRP (primarily through exposure to calcium) while a minority used non-activated PRP. Different preparatory methods of PRP as well as different numbers of treatments across varying periods make it difficult to generalize the parameters that promote hair growth using PRP.

Outcomes also varied between studies from those that used wholly qualitative, subjective analyses to those that used a variety of quantitative assessments. Among those with quantitative outcomes (such as hair density and hair count), the methods of counting hair and the intervals of follow-up were not reported uniformly. As a result, we could only attempt to include three studies[32,35,36] in the aforementioned meta-analysis, which ultimately showed significant heterogeneity.

This systematic review suggests that PRP may be a promising new treatment for AGA and readily implicates areas of future research. First, the optimum use of PRP in terms of preparation, activation, and treatment regimens is unknown. Dohan Ehrenfest et al describe a classification system of platelet concentrates based on preparatory process and leukocyte and fibrin content: pure platelet-rich plasma (P-PRP), leukocyte- and platelet-rich plasma (L-PRP), pure platelet-rich fibrin (P-PRF), and leukocyte and platelet-rich fibrin (L-PRF).[41] Anitua et al used a P-PRP system.[15] Tawfik et al,[34] Farid et al,[33] Jha et al,[16] Kachhawa et al,[17] Rodrigues et al,[20] Singhal et al,[22] and Khatu et al[24] used L-PRP based on descriptions of their preparations that included the buffy coat in their second step hard spin centrifugation. Gentile et al,[30] Borhan et al,[21] Betsi et al,[27] Gkini et al,[23] and Kang et al[37] referenced L-PRP systems (Regen or SmartPrep), but newer kits could variably generate L-PRP or P-PRP. Sclafani created a platelet-rich fibrin matrix that approximates P-PRF.[26] The remaining articles do not name specific preparatory kits or describe methods that fit easily within this system. Thorough exploration of the preparation processes and systems used may help elucidate the most effective platelet concentrate technology for hair regeneration.

Second, as patients with AGA can be affected from a young age, longer follow-up of patients is required to determine whether this treatment has long-lasting effects or whether repeated injections could be considered. Third, only 28% of patients in this systematic review were female and there remains limited information on potential gender differences in the effect of PRP. Lastly, the basic biological activity of PRP should be further explored. Many growth factors have been identified in PRP including platelet-derived growth factor, transforming growth factor-β, vascular endothelial growth facture, epidermal growth factor, and insulin-like growth factor. These growth factors are present in much higher concentrations (by a factor of five to eight times) in PRP than in whole blood, and PRP has been preliminarily shown to induce the proliferation of dermal papilla cells by upregulating fibroblast growth factor-7 (FGF-7), β-catenin, and extracellular-regulated kinase (ERK)/Akt signaling.[42] The precise biological pathways by which PRP promotes hair restoration remain unverified.

Conclusion

This is the first systematic review in the facial plastic surgery literature dedicated to the use of PRP for hair restoration in patients with AGA. Out of 24 studies, 21 reported positive outcomes using PRP, with outcome measures ranging from qualitative photographic assessments to quantitative hair counts and hair density evaluations. Further research methodically examining the patient populations that benefit most from this treatment, optimizing preparation and administration procedures and following up long-term outcomes, is needed. PRP appears to be a safe technology with the potential for promoting hair restoration.

Conflicts of Interest
None.

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