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ORIGINAL ARTICLE NON-SURGICAL AESTHETICS

# Platelet-Rich Plasma for Treating Androgenic Alopecia: A Systematic Review

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**Abstract**

*Background* Platelet-rich plasma (PRP) contains a variety of growth factors and proteins that can accelerate tissue repair. Androgenic alopecia is a genetic disorder characterized by atrophy of hair follicles and hair loss. At present, PRP injections for hair restoration have become a popular though controversial practice. We conducted a meta-analysis to compare the differences between patients treated with local injections of PRP and control group subjects to explore the effectiveness of PRP treatment for androgenic alopecia.

*Materials and Methods* We searched PubMed, EMBASE and the Cochrane Library until Jan 2019 for human studies evaluating the efficacy of PRP for the treatment of androgenic alopecia.

*Results* We retrieved 132 papers; 11 articles matched our inclusion criteria and comprised 262 androgenic alopecia patients. Through a meta-analysis, we found a significantly locally increased hair number per $cm^2$ after PRP injections in the treatment group versus the control group (mean difference 38.75, 95% CI 22.22–55.28, $P < .00001$). Similarly, a significantly increased terminal hair density was found in the PRP group compared with the control group (mean difference 22.83, 95% CI 0.28–45.38, $P = 0.05$).

*Conclusion* Most studies suggest that subcutaneous injection of PRP is likely to reduce hair loss, increase hair diameter and density in patients with androgenic alopecia. Because of the low quality of the studies, small sample sizes, different treatment regimens and possible publication bias, the results of this meta-analysis should be interpreted with caution. Furthermore, more randomized controlled studies should be performed.

*Level of Evidence III* This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

**Keywords** Androgenic alopecia · Platelet-rich plasma · Meta-analysis

## Introduction

Androgenic alopecia (AGA) is the most common type of hair loss. It is a hereditary disease, and about half of the population suffers from it. The pathogeny of the illness is that the scalp hair follicles of patients are sensitive to dihydrotestosterone, which causes hair follicles to shrink and gradually disappear, resulting in hair loss [1]. For patients, hair loss affects not only their appearance but also their psychology, and there is a high prevalence of depression in AGA patients [2].

Platelet-rich plasma (PRP) is an autologous product manufactured by the centrifugation of a patient's own venous blood. The normal human platelet count number is 1.5–4.5 $\times$ $10^5$/ml, whereas the count in PRP is about four to five times higher than that in normal plasma. PRP contains various growth factors, including platelet, epidermal, transforming, fibroblast, insulin-like and vascular

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endothelial growth factors; these factors interact with each other and promote tissue healing in wound [3].

In the treatment of AGA, finasteride and minoxidil are widely used and approved by the Food and Drug Administration. Other treatments such as those involving interfollicular placental extract, polydeoxyribonucleotide and microneedle devices are also used. To verify the effect of PRP on AGA, several studies have been conducted; however, the conclusions have been controversial.

To evaluate the efficacy of subcutaneous injection of PRP in patients with AGA, we performed a comprehensive meta-analysis.

## Materials and Methods

### Search Strategy

Two authors individually carried out a full systematic literature search of PubMed, the Cochrane Library and EMBASE for any study on PRP use for hair growth therapy in AGA until April 2018; then, we updated the data on January 12, 2019. To identify studies involving AGA patient populations, we searched "Alopecia", "Baldness", "Hair Loss", "Hair Losses", "Loss, Hair", "Losses, Hair", "Alopecia, Male Pattern", "Male Pattern Alopecia", "Baldness, Male Pattern", "Male Pattern Baldness", "Female Pattern Baldness", "Baldness, Female Pattern", "Androgenetic Alopecia", "Pattern Baldness", "Baldness, Pattern", "Androgenic Alopecia", "Alopecia, Androgenic", "Alopecias, Androgenic", "Androgenic Alopecias", "Alopecia, Androgenetic", "Pseudopelade", "Alopecia Cicatrisata", "Alopecia Cicatrisatas", "hair growth", "hair restoration", "female pattern hair loss", and "pattern hair loss". Then, to identify studies involving a PRP intervention, we searched "Platelet-Rich Plasma", "Plasma, Platelet-Rich", "Platelet Rich Plasma", and "PRP". Groups were connected with "and". In the same group, the words were connected with "or". To reflect the principle of control, using the McMaster University searching strategy, we searched " (clinical [Title/Abstract] AND trial [Title/Abstract]) OR clinical trials as topic [MeSH Terms] OR clinical trial [Publication Type] OR random* [Title/Abstract] OR random allocation [MeSH Terms] OR therapeutic use [MeSH Subheading]" in PubMedand, "'random':ab,ti OR 'clinical trial':ti,ab OR'health care quality'/exp" in EMBASE. No language restrictions were applied. All authors' search results were merged to remove duplicate articles.

### Study Selection

The included studies followed the patients, intervention, comparator, outcomes, and study design (PICOS) principle. We selected only those studies that concerned AGA; that included an experimental group treated with subcutaneous injection of PRP alone; and that had a control group that was restricted to negative controls, such as normal saline. We excluded duplicate articles, reviews, animal experiments, comments, letters, case reports, hair transplant surgeries, conference abstracts, and in vitro studies. Studies of alopecia areata and other kinds of hair loss were also excluded. Two coauthors evaluated the studies independently; then, they worked together to ensure that each study could be included.

### Data Extraction

The data collected from each article were extracted by three researchers. Differences in the collected data were resolved by consensus. The data included the following points: first author, study type, sample size, patient characteristics, study design, assessment method, PRP preparation method, and complications. All randomized controlled trials (RCTs) were graded using the Cochrane Collaboration's risk of bias assessment tool [4]. The research group met to resolve any differences in the assessment and to reach a consensus. The primary outcome was hair density. The secondary outcome was hair cross section. The third outcome was terminal hair density. Other outcomes included vellus hair density, hair loss, patient satisfaction survey, and side effects.

### Statistical Analysis

The weighted mean difference (MD) with 95% CI was used to analyze the measurement data. Heterogeneity was evaluated by using the $I^2$ statistic, which describes the differences between studies. We employed random-effects analysis in all studies because of the study design difference. $P \leq 0.05$ was considered statistically significant. Publication bias was assessed by funnel plot analyses. Review Manager 5.3 software was used for all statistical analyses in this study.

## Results

The search retrieved 132 articles. Of these papers, 121 were excluded for the following reasons: 33 articles were duplicates; 11 did not have a control group; 8 did not have a negative control; 9 were meta-analyses; 8 were not concerned with AGA; 5 were comments; 30 were reviews;

2 were animal experiments or in vitro experiments; 3 were conference abstracts; 1 was a letter; 1 was a hair transplant surgery; and 10 were abstracts only. Finally, 11 papers were included in this review [5–15]. The flowchart is presented in Fig. 1. The experimental method and results are presented in Tables 1 and 2.

In total, 262 AGA patients, comprising 179 males and 83 females, were collected in the 11 [5–15] studies; the patients ranged in age from 18 to 65 years. All the male characteristics of alopecia were Norwood–Hamilton classification stage II–VI, whereas the female characteristics were Ludwig classification stage I–III. Some studies were controlled clinical trials (CCTs) [5, 6, 8, 13, 15], whereas the others were RCTs [7, 9–12, 14], which were assessed by the Cochrane Collaboration's tool for assessing risk of bias shown in Fig. 2.

These studies used hair density, hair thickness, vellus/terminal hair ratio, anagen/telogen hair ratio, histopathology, patient satisfaction, hair loss, pull test and side effects to evaluate the differences between the experimental group and the control group before and after treatment.

## Hair Density

Ten articles except Mohammad Ali Mapar [10] discussed the difference in hair density before and after treatment. Two of them [8, 11] considered the treatment ineffective, while the others [5–7, 9, 12–15] considered it effective. Abaroa [8], Puig [11], Kachhawa [13] and Rodrigues [15] did not provide specific data in their papers, but the remaining 6 articles [5–7, 9, 12, 14] were included in the pooled analysis, which showed a significant difference in the number of hairs per $cm^2$ between the experimental and control groups ($n$ = 113, MD = 38.75, $I^2$ = 80%, 95% CI 22.22–55.28, $P < 0.00001$, Fig. 3; funnel plot, Fig. 4); when all the CCTs (Takikawa [5], Cervelli [6]) were excluded, similar results were obtained ($n$ = 90, MD = 49.78, $I^2$ = 63%, 95% CI 36.25–63.30, $P < 0.00001$, Fig. 5; funnel plot, Fig. 6). However, a large statistical heterogeneity was found in the analysis, indicating important differences in study designs; in addition, the funnel plot showed that there was publication bias.

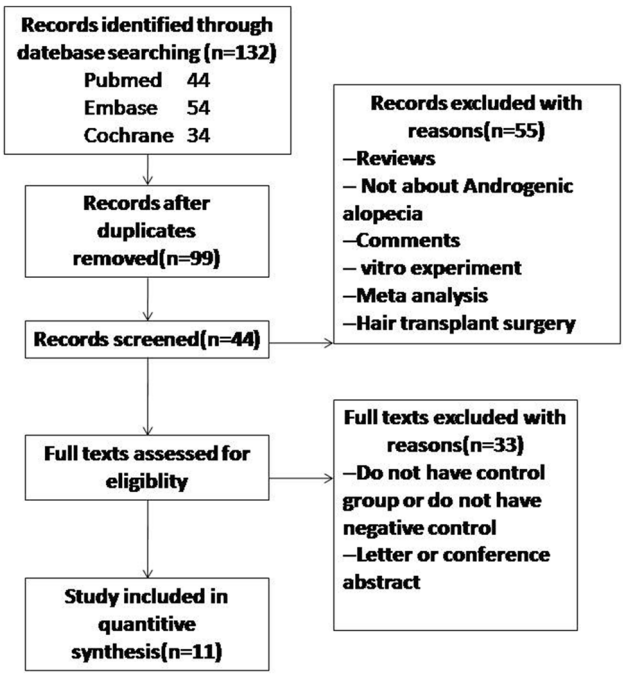


**Fig. 1** Flowchart of review results

## Hair Cross Section

Four articles discussed the effect of PRP on hair cross section: 3 [5, 12, 13] considered the treatment effective, and one [8] showed that hair cross section was improved after treatment, but the results were not statistically significant. All the experimental results are presented in Table 2.

## Terminal Hair Density

Five studies [6, 7, 9, 10, 15] discussed terminal hair density before and after treatment. The experimental results are presented in Table 2. Two studies [10, 15] considered the treatment ineffective but did not provide specific data in their papers, the remaining three studies were included in the pooled analysis, which showed a significant difference in the number of terminal hairs per $cm^2$ between the experimental and control groups ($n$ = 52, MD = 22.83, $I^2$ = 32%, 95% CI 0.28-45.38, $P$ = 0.05, Fig. 7; funnel plot, Fig. 8).

## Other Endpoints

Five studies [6, 7, 9, 10, 15] discussed the effect of PRP on vellus hair density, all of them considered the treatment ineffective. Three studies used patient satisfaction surveys or hair shedding to evaluate the efficacy of PRP treatment. Puig [11] discovered that 13.3% of the treatment subjects (vs 0% of the placebo subjects) claimed to have improved hair thickness and reduced hair loss, 26.7% of the patients in the study group (vs 18.2% of the control subjects) claimed that after the treatment, their hair became heavier. Kachhawa [13] showed that at baseline, the mean number of hairs pulled was eight, while at the third treatment, the pull test reached normal levels (control group not mentioned); 70% of patients claimed an improvement in hair quality and thickness, and 55% reported an increase in hair density. Tawfik [14] discovered that before treatment, all the patients had a positive hair pull test and that after the

**Table 1** Characteristics of included studies

| Author | Study type | Sample size male/female | Patient characteristics | Half head | Experimental group | Control group | Experimental method/Injection dose | Assessment method | PRP preparation/platelet counts | Complications |
|---|---|---|---|---|---|---|---|---|---|---|
| Takikawa [5] 2011 | CCT | 26 (16/10) | NA | Yes | PRP | Saline | Five injections at weeks 0, 2, 4, 6, and 9/NA | Dermoscopy, Digital camera, Histologic examination | 15 mL blood, 1700 rpm × 15 min for 1st centrifugation, then 3000 rpm × 5 min for 2nd centrifugation. Not activated/ 88.2 ± 21.7 × $10^4$µl | Temporary pain |
| V. Cervelli [6] 2014 | CCT | 10 (10/0) | Norwood–Hamilton classification stage IIa–IV | Yes | PRP | Saline | Three injections at weeks 0, 4, and 8/0.1 ml/$cm^2$ | Global photography, Physician's and patient's global assessment scale, Standardized photo trichograms | 18 cc blood, 1100 rpm × 10 min. Activated by Ca2 +/NA | NA |
| Gentile [7] 2015 | RCT | 23 (23/0) | Norwood–Hamilton classification stage IIa–IV | Yes | PRP | Saline | Three injections at intervals of 30 days/ 0.1 ml/$cm^2$ | Computerized trichogram, Microscopic evaluation | 60 ml of blood, 1200 rpm × 10 min. Activated by Ca2 +/NA | NA |
| Abaroa [8] 2016 | CCT | 20 (14/6) | NA | No | PRP | distilled water | Six injections, two times a week for three weeks/ 0.2 ml/$cm^2$ | Video camera, Histologic Examination | 20-30 ml blood, 1800 rpm × 10 min for 1st centrifugation, 3000 rpm × 10 min for 2nd centrifugation. Activated by Ca2 +/NA | NA |
| Alves [9] 2016 | RCT | 22 (11/11) | Male: Hamilton–Norwood II–V Female: Ludwig classification I–III | Yes | PRP | Saline | Three injections at intervals of 1 month/ 0.15 mL/$cm^2$ | Global photography, Phototrichogram | The 20 mL citrated blood, 460 g × 8 min for 8 min. Activated by Ca2 +/ 1.523.82 ± 35,000 platelets/uL | Temporary pain at the injection site |
| M apar [10] 2016 | RCT | 17 (17/0) | Hamilton–Norwood IV–VI | Yes | PRP | Saline | Two injections at intervals of 1 month/1.5 ml in 2.5 × 2.5 cm | NA | 9 ml blood, 3000 rpm × 6 min for 1st centrifugation, then 3000 rpm × 3 min for 2nd centrifugation. Activated before use/ 572 × $10^3$platelets/µl | NA |

**Table 1** continued

| Author | Study type | Sample size male/female | Patient characteristics | Half head | Experimental group | Control group | Experimental method/Injection dose | Assessment method | PRP preparation/platelet counts | Complications |
|---|---|---|---|---|---|---|---|---|---|---|
| Puig [11] 2016 | RCT | 26 (0/26) | Ludwig classification II | No | PRP | Saline | One injection/10 ml in 10 × 10 cm | Photography, Cohen hair check system, Patient survey | Using the Angel PRP system, not activated./2.75 to 3.4X platelet concentration | NA |
| Gentile [12] 2017 | RCT | 18 (18/0) | Hamilton–Norwood II–IVa | Yes | PRP | Saline | Three injections at intervals of 1 month/NA | Video-epiluminescence microscopy, Digital image analysis | 55 ml of whole blood, 1200 rpm × 10 min. Not activated/NA | NA |
| Kachhawa [13] 2017 | CCT | 44 (44/0) | Hamilton–Norwood III–VI | Yes | PRP | Saline | Six injections at intervals of 21 days/1-2 cc in 1 × 1 cm | TrichoScan software | 16 ml blood, 1200 rpm × 8 min for 1st centrifugation, then 2400 rpm × 4 min for 2nd centrifugation. Not activated/NA | Pain at the injection site |
| Tawfik [14] 2017 | RCT | 30 (0/30) | Ludwig classification I–III | Yes | PRP | Saline | Four injections at intervals of 1 week/NA | Global photography, Hair pull test, Patient's satisfaction scale, Standardized phototrichograms | 10 ml blood, 1200 rpm × 15 min for 1st centrifugation, then 2000 rpm × 10 min for 2nd centrifugation. Activated by calcium gluconate before use/NA | Temporary pain and bleeding |
| Rodrigues [15] | CCT | 26 (26/0) | Hamilton–Norwood III | No | PRP | Saline | Four injections at intervals of 15 days/2 ml every time | TrichoScan | Using the methodology of Amable. Activated by Ca2 +/1200 × $10^6$ platelets/μl | NA |

*NA* not available

**Table 2** Results of included studies

| Author | Object measure | Results |
|---|---|---|
| Takikawa [5] 2011 | Hair density | The PRP group showed a greater mean number of hairs and different hair diameter than the control group after the fifth injection ($P < 0.01$) |
| | Hair diameter | |
| | Histologic examination | Thickened epithelium, proliferation of collagen fibers and fibroblasts, and more numbers of blood vessels around hair follicles in the PRP group |
| Cervelli [6] 2014 | Hair density vellus hair/terminal hair ratio | The PRP group exhibited a greater mean number of hairs than the control group ($P < 0.0001$) |
| | Histological evaluation | The terminal hair density improved significantly in the PRP group but not in the control group |
| | Immunohistochemistry | No significant differences in vellus hair density between the study and control groups |
| | | Microscopic evaluation showed an increase in epidermis thickness, a greater number of follicles, a slight increase in small blood vessels around hair follicles, and an increase in Ki67 + basal keratinocytes of the epidermis and of hair follicular bulge cells. |
| Gentile [7] 2015 | Hair density | An increase in hair density was observed in the experimental group and a decrease in the control group ($P < 0.0001$) |
| | Vellus hair/terminal hair ratio | |
| | Histological evaluation | The terminal hair density improved significantly in the PRP group but not in the control group |
| | Immunohistochemistry | No significant differences in vellus hair density between the study and control groups |
| | | Microscopic evaluation showed an increase in epidermis thickness and the number of follicles. Immunohistochemistry showed an increase in Ki67 + basal keratinocytes of the epidermis and of hair follicular bulge cells when compared with baseline. |
| Abaroa [8] 2016 | Hair number | No significant difference was observed in the number, thickness and level of follicles in the anagen or/catagen ratio between the group receiving APRP and that receiving placebo. |
| | Hair thickness | |
| | Level of follicles in the anagen or/catagen ratio | |
| Alves [9] 2016 | Hair density | Compared with the control, platelet-rich plasma was found to increase hair density, the mean anagen hairs, telogen hairs, terminal hair density |
| | Terminal hair density Anagen (%) | |
| | Telogen (%) | No differences in vellus hair density between the PRP and placebo groups were observed |
| | Anagen/telogen ratio | |
| Mapar [10] 2016 | Terminal hair count | No differences were observed in terminal and vellus hair count between the PRP and control groups |
| | Vellus hair count | |
| Puig [11] 2016 | Patient survey | There was no difference in hair count between the experimental and control groups |
| | Hair count | The patient survey results suggested a therapeutic advantage of PRP as perceived by patients but not according to hair count or HMI |
| | Hair mass index | |
| Gentile [12] 2017 | Hair count | Both the hair count and hair density were significantly improved in the experimental group compared to the control group |
| | Total hair density | |
| | Hair diameter | Microscopic evaluation conducted two weeks after treatment showed an increase in epidermal thickness, Ki67 + keratinocytes, and the number of follicles |
| | Histological evaluation | |
| Kachhawa [13] 2017 | Hair thickness | Using TrichoScan software, they discovered an improvement in hair density and quality in the experimental group, which was significantly different from the control ($P < 0.05$). Hair pull test reached normal levels. Seventy percent of patients reported an improvement in hair quality and thickness, while 55% reported an increase in hair density |
| | Hair density | |
| | Hair pull test | |
| | Patient survey | |
| Tawfik [14] 2017 | Hair growth | There was a significant difference between the PRP and placebo groups ($P < 0.005$) regarding both hair density and hair thickness as measured by a folliscope. |
| | Hair density | |
| | Hair diameter | The hair pull test became negative in PRP-injected areas in 25 patients (83%) with an average number of three hairs. Global pictures showed a significant improvement in hair volume and quality together with a high overall patient satisfaction in PRP-injected sites, and these results were maintained during the 6-month follow-up |
| | Volume | |
| Rodrigues [15] | Hair count | Both the hair count and hair density were significantly improved in the experimental group compared to the control group |
| | Hair density | |
| | Anagen (%) | Compared with baseline and 15 days after the last injections, the anagen percentage was significantly increased in the PRP group. However, at 3 months after the last injections, this result was not maintained, and the control group showed no significant increase at any of the evaluated time points |
| | Telogen (%) | |
| | Terminal/vellus hair ratio | |

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6-month follow-up, the pull test was negative in 83% of the PRP group patients but positive in all the subjects in the control group. Rodrigues [15] compared with the baseline and 15 days after the last injections, the anagen percentage was significantly increased in the PRP group. However, at 3 months after the last injections, this result was not maintained, and the control group showed no significant increase at any of the evaluated time points.

A histological or immunohistochemisty examination was performed in 5 studies [5–8, 12] to evaluate the histological changes under subcutaneous injection of PRP. All of the authors agreed that compared with a control treatment, the injection of PRP made the epidermis thicker, collagen fibers and fibroblasts proliferate, and the number of hair follicles and blood vessels around these fibers increase; in addition, immunohistochemisty showed an increase in Ki67 + basal keratinocytes of the epidermis and of hair follicular bulge cells when compared with baseline, indicating cell proliferation of the hair skin.

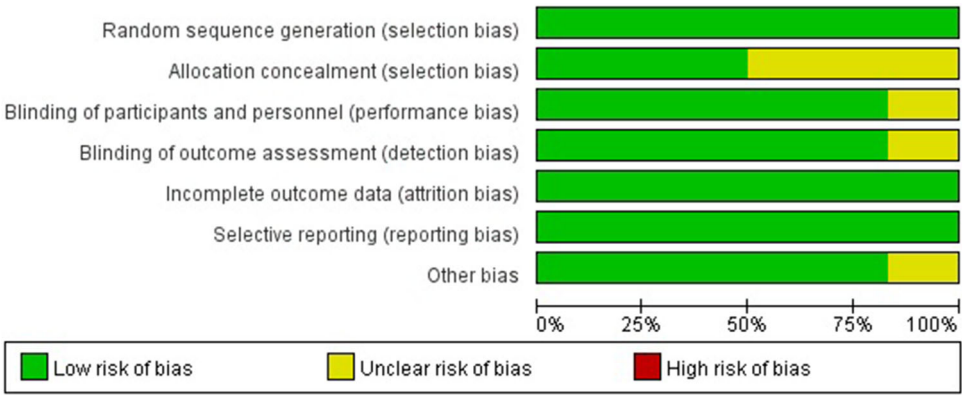


**Fig. 2** Risk of bias among controlled clinical trials

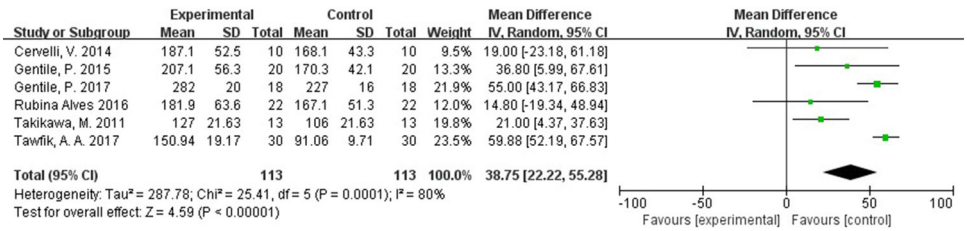


**Fig. 3** Forest plot showing the increased hair density compared with control

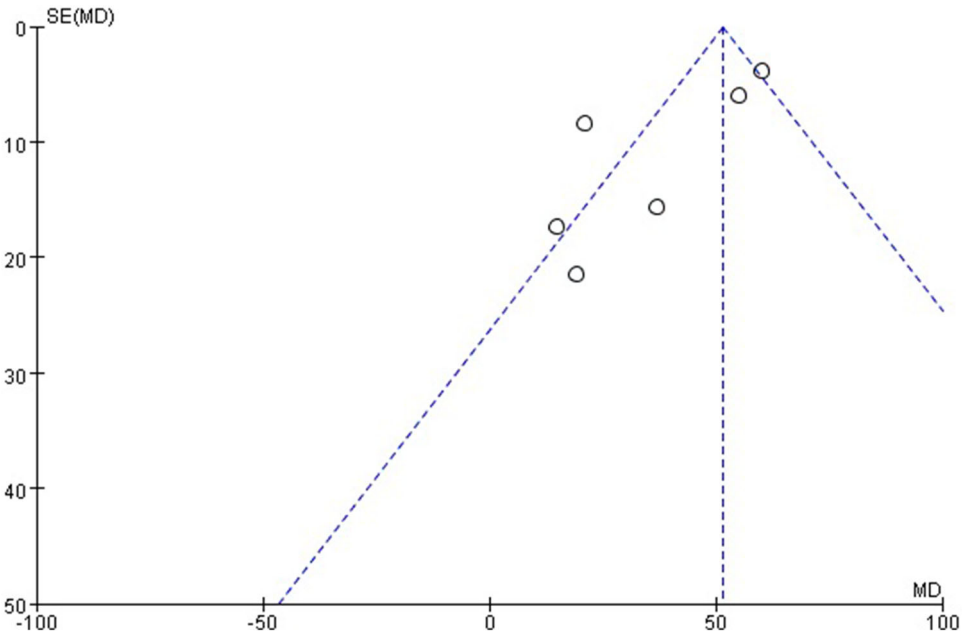


**Fig. 4** Funnel plot for bias assessment in hair density increase

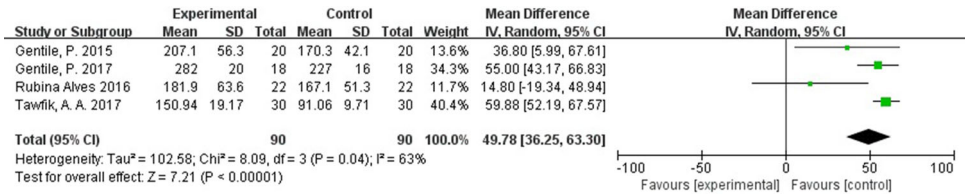


**Fig. 5** Forest plot showing the increased hair density compared with control among RCT studies

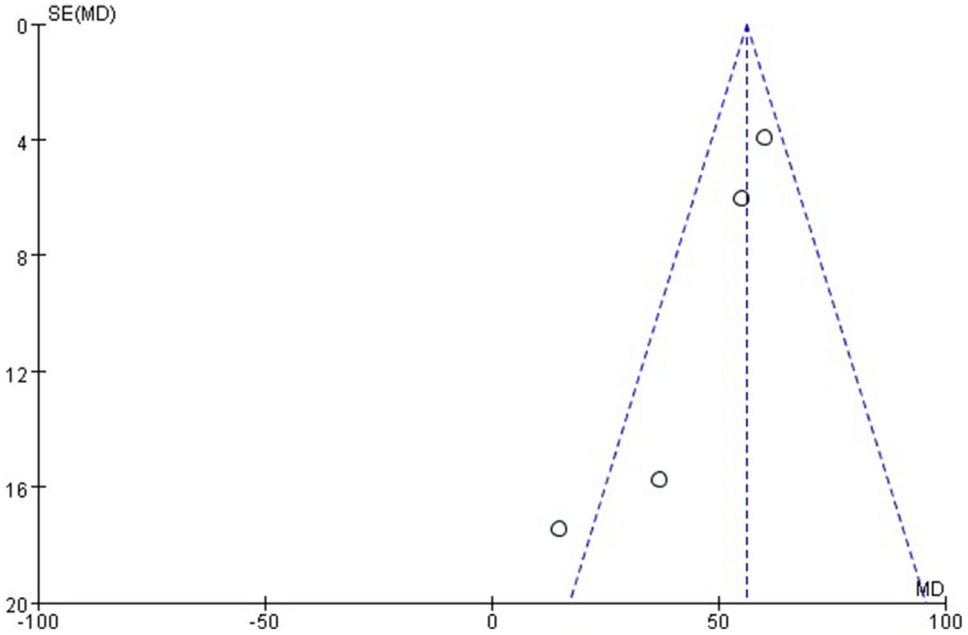


**Fig. 6** Funnel plot for bias assessment in hair density increase among RCT studies

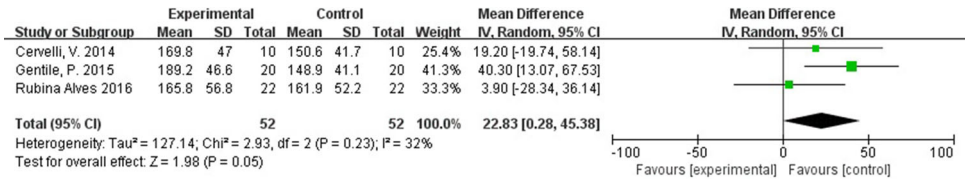


**Fig. 7** Forest plot showing the increased terminal hair density compared with control

Some of the studies provided the complications during PRP treatment, and temporary pain at the injection site and bleeding were most often mentioned; some papers also referred to transient post treatment edema and tenderness, mild itching, and desquamation.

## Discussion

AGA is the most common cause of alopecia because the inhibitory effect of dihydrotestosterone causes hair follicle miniaturization. Normally, the treatment includes oral finasteride and topical minoxidil. However, long-term treatment and side effects give a negative impact on the use of drugs.

PRP is an autologous product manufactured from a patient's own venous blood, so cross-contamination and immune reactions will not happen. Through centrifugation, the platelet concentration can rise to three- to eight fold higher than that in normal peripheral blood [16]; likewise, growth factors [17], excreted by the a-granules of concentrated platelets, including platelet-derived growth factor (PDGF), transforming growth factor (TGF), vascular endothelial growth factor (VEGF), and epidermal growth factor (EGF), increase. These growth factors are thought to play an important role in hair growth. Li [18] discovered that after concentrating human venous blood, there were approximately 8.8 times more platelets in PRP than in whole blood and that PRP induces the proliferation of dermal papilla (DP) cells and increases phosphorylated extracellular signal-regulated kinases (pERKs) and Akt expression in DP cells, which induces cell growth, promotes cell survival and prevents apoptosis in vitro. Additionally, PRP increases the levels of the antiapoptotic protein Bcl-2, which modulates the expression of apoptotic molecules and contributes to cell survival.

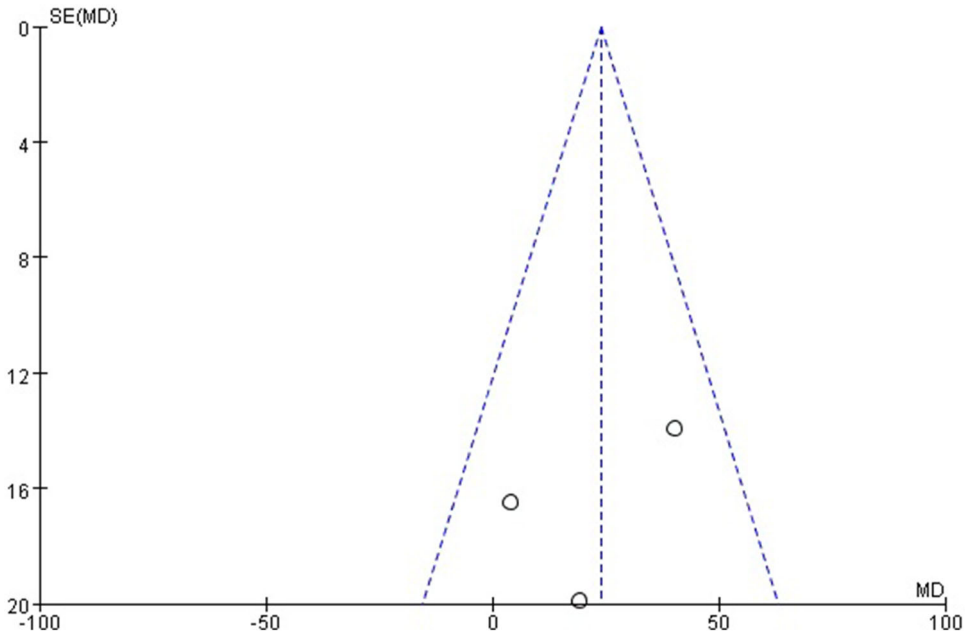


**Fig. 8** Funnel plot for bias assessment in terminal hair density increase

Although it is not yet recommended, given the above findings, researchers have tried to make use of PRP to treat AGA and to clarify its role in treatment. At present, there have been many clinical studies, but most of them are low quality because they either lack a control group or have no accurate evaluation method; in addition, the PRP preparation methods in these studies are different, and the number of patients included in the studies is small. These limitations affect the evaluation of the treatment. Therefore, we set the retrieval conditions to eliminate low-quality studies, and finally, 11 studies describing 262 patients were included in our meta-analysis.

Through statistical analysis, we found that the number of hairs per $cm^2$ and the terminal hair density were increased after treatment with PRP (Figs. 3, 5, 7), however, the treatment is not likely to increase vellus hair density. Additionally, though not included in the statistical analysis, most of the studies also suggested that hair cross section was increased after PRP treatment.

Ehrenfest [19] classifies PRP into 4 types: P-PRP, which includes no leukocytes and low-density fibrin; L-PRF, which includes leukocytes and low-density fibrin; P-PRF, which includes no leukocytes and high-density fibrin; and L-PRF, which includes leukocytes and high-density fibrin. The kind of PRP more effective in promoting hair growth has not yet been confirmed. None of the studies we included in the present meta-analysis mentioned which kind of PRP was used, and there is no unified process for the preparation of PRP; different protocols have different numbers of spins, time periods of centrifugation and ranges of centrifugal acceleration. However, all of the studies followed the sequence of blood collection, separation of RBCs and concentration of platelets. Giusti [20] discovered the optimal concentration of platelets was $1.5 \times 10^6/\mu L$; excessively higher or lower platelet concentrations may inhibit the process of hair growth. Rodrigues [15] discovered that the injection of PRP can increase hair count, hair density and percentage of anagen hairs but failed to find an association between platelet count, PDGF, EGF, VEGF levels and clinical improvement. Dhurat [21] summarized studies and recommended that the optimum protocol was $900\times g$ for 5 min for the 1st centrifugation then $1000\times g$ for 10 min for the 2nd centrifugation at 16 °C. It is also controversial whether PRP needs to be activated before use; Ince [22] made a comparison between activated and nonactivated PRP for treating AGA; they discovered hair density with nonactivated PRP was greater than with activated groups. Leitner [23] thought that not only through prior activation before injection could hair follicles obtain growth factors but also by using endogenous activation, slower and more efficient elements could be obtained.

In our review, we found that researchers used centrifugation speeds from 1100 to 3500 rpm; 6 [5, 8, 10, 13–15] studies used double centrifugation, 4 [6, 7, 9, 12] used single centrifugation, and 1 [11] used a commercial kit. As 7 [5–7, 9, 12, 14, 15] studies used hair density as an assessment criterion, in the pooled analysis, we contrasted the MD between the single and double centrifugation groups and found that the MD ($n$ = 70, MD = 36.37 95% CI 14.80–57.59, $P$ = 0.06, $I^2$ = 59%) of hair density for single-spin centrifugation was lower than that for double-spin centrifugation ($n$ = 43, MD = 41.17 95% CI 3.09–79.24, $P < 0.0001$, $I^2$ = 94%); however, a large statistical heterogeneity and the $P$ value in single-spin group

made the contrast meaningless. Then, we compared the MDs of $Ca^{2+}$-activated studies [6, 7, 9, 14, 15] and no-activation studies [5, 12] and did not find any difference between them (MD 36.87 vs 38.52). Due to high statistical heterogeneity and small sample sizes, in terms of promoting hair density, we failed to see any difference between centrifugation methods and the effect of activation on the experiment.

There was also no uniform frequency and interval of PRP injection. Farid [24] made a comparison between PRP and 5% topical minoxidil and discovered that both treatments promoted hair growth; however, the minoxidil group showed significant improvement at 12 weeks, whereas the PRP group showed significant improvement at 16 weeks, indicating that PRP treatment has a slow onset. The author recommended that the treatment interval can be shortened in the first 12 weeks. In our review, PRP treatment was given at least [11] once and at most [8, 13] 6 times; the shortest [8] treatment interval was 3 days, whereas for most studies a 1-month interval was chosen. Disappointingly, we failed to find a connection between the frequency, interval and treatment effects; furthermore, compared with other studies, Abaroa [8] used the shortest interval and greatest number of treatments but achieved negative results, which is confusing.

Normally, the treatment options for AGA vary with the severity of the disease. Treatment guidelines [25] for AGA suggest that oral finasteride or topical minoxidil is suitable for mild to moderate AGA (Hamilton–Norwood II–V); however, the hair follicles of patients with more severe AGA shrink and gradually disappear and cannot regenerate. Therefore, we speculate that compared to oral finasteride or topical minoxidil, PRP is equally ineffective in the treatment of severe AGA (Hamilton–Norwood V–VI). In this review, most papers described patient characteristics, and we found that the negative studies [10, 11] happened to include some patients with severe AGA (Hamilton–Norwood IV–VI Ludwig classification II). We believe that similar to finasteride or minoxidil, PRP is not suitable for the treatment of severe AGA.

Few articles describe the long-term efficacy of PRP in the treatment of AGA. Gentile [12] reported that some patients tended to have a relapse of AGA when PRP treatment was stopped. AGA is a hereditary disease, which means that it cannot be completely cured; therefore, similar to oral finasteride or topical minoxidil treatment, once PRP injections are stopped, a relapse of AGA will occur.

Unlike oral finasteride, subcutaneous injection of PRP has no side effects such as sexual dysfunction; however, mild side effects include temporary pain at the injection site, transient post treatment edema and tenderness, mild itching, desquamation, headache, and bleeding. The fewer side effects associated with PRP injections compared with those for oral finasteride treatment increased patient enthusiasm for PRP treatment.

## Conclusion

Most of the studies (8/11) reviewed in this meta-analysis suggest that PRP is effective in treating AGA and is likely to reduce hair loss, increase hair diameter and density. These views have been supported in some in vivo studies and histological examinations. In addition, the side effects of PRP treatment are mild. These findings highlight the promise of PRP injections as a new treatment for AGA. However, most of the studies were non-RCTs with small sample sizes that had different patient ages and illness severities, different PRP preparation methods, different treatment regimens (treatment intervals and frequencies), and different control groups (half head or full head). These discrepancies led to large statistical heterogeneity in the meta-analysis; furthermore, the funnel plot implied the possibility of publication bias. Therefore, although the statistical analysis showed that PRP is effective for treating AGA, we should interpret this finding with caution. Furthermore, questions related to whether PRP must be activated before injection, the optimal PRP preparation method, the optimal frequency and treatment interval, and the long-term efficacy of PRP treatment must be answered. To investigate the efficacy and safety of PRP in treating hair loss, more RCTs are required, with standard protocols concerning more objective evaluation of hair loss, the number and interval of treatment sessions, the number of platelets, the method of activation and the long-term follow-up outcomes.

#### Compliance with Ethical Standards

**Conflict of interest** The authors declare that they have no conflicts of interest to disclose.

**Human and Animal Rights** This article does not contain any studies with human participants or animals performed by any of the authors.

**Informed Consent** For this type of study informed consent is not required.

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