





Autologous platelet-rich plasma therapy for pattern hair loss: A systematic review

Gezim Dervishi¹ | Haibo Liu MD²  | Sandra Peternel MD, PhD^{3,4}  |
Alexander Labeit MD, Dr. rer. pol.⁵  | Frank Peinemann MD, PhD, MSc, MSc^{1,6} 

¹Children's Hospital, University Hospital
Cologne, Cologne, Germany

²Department of Dermatology, Jinling
Hospital, Nanjing University School of
Medicine, Nanjing, China

³Department of Dermatovenerology, Clinical
Hospital Centre Rijeka, Rijeka, Croatia

⁴Faculty of Medicine, University of Rijeka,
Rijeka, Croatia

⁵Saw Swee Hock School of Public
Health, National University of Singapore,
Singapore, Singapore

⁶FOM University of Applied Science for
Economics & Management, Essen, Germany

Correspondence

Frank Peinemann, Children's Hospital,
University of Cologne, Kerpener Str. 62,
50937 Cologne, Germany.
Email: pubmedprjournal@gmail.com

Abstract

Background: Androgenetic alopecia (male pattern and female pattern hair loss) is characterized by thinning of the scalp hair. Intradermal injection of autologous platelet-rich plasma (PRP) might have an effect on hair regrowth.

Aims: The aim was to evaluate efficacy and safety of platelet-rich plasma compared to placebo or no treatment in people with pattern hair loss.

Patients/Methods: We searched the databases CENTRAL and MEDLINE on December 24, 2018 and included randomized controlled trials (RCTs). Primary outcomes were mean change of hair density from baseline and serious treatment-related adverse events. Secondary outcome was mean change of hair thickness from baseline. Time point of outcome assessment was 6 months after start of treatment.

Results: We identified 13 relevant randomized controlled trials with 356 randomized (343 analyzed) people or half-head areas who received PRP in a simple parallel or half-head design. The pooled data of seven studies (171 analyzed people or half-head areas) were favorable in the PRP group on hair density. We estimated a mean difference from baseline of 30.35 associated with a wide 95% confidence interval (1.77-58.93), a considerable heterogeneity ($I^2 = 100\%$), and unclear risk of bias in most of the studies. Regarding hair thickness, data were also favorable in the PRP group, but these data were limited to a single study. We did not identify serious treatment-related adverse events.

Conclusion: The results of seven RCTs indicated that autologous platelet-rich plasma was associated with an increase of hair density when compared to placebo.

KEYWORDS

androgenetic alopecia, pattern hair loss, platelet-rich plasma, systematic review

1 | INTRODUCTION

Androgenetic alopecia, also known as male pattern and female pattern hair loss, is the most common cause of hair loss.¹ It is characterized by progressive thinning of the scalp hair expressed by a reduction in hair density.² Male pattern hair loss is believed to be a genetically determined sensitivity to androgen action. It presents

with a typical pattern of bitemporal and frontal recession of the hair line which can be followed by thinning of the vertex. It may progress to a complete alopecia of the crown with the sides are generally spared, possibly due to a different response to androgens.^{3,4} Severity of male pattern hair loss is categorized by the Hamilton-Norwood classification.⁵ The prevalence increases with age, from 30% for men in their 30 seconds to 50% for men in their

50 seconds.¹ In the course of their life, 80% of men may be affected.⁶ Female pattern hair loss has a more complicated etiology, and the requirement of androgens is less clear-cut. It presents with diffused hair loss in the centroparietal area with sparing of the frontal hair line.⁷ Severity of female pattern hair loss is categorized by the Ludwig classification.⁸ The prevalence is estimated at 25% for women in their 50 seconds.¹ In the course of their life, 50% of women may be affected.⁶ Pattern hair loss in adolescents was reported in a retrospective review of 57 people.⁹ Most observed participants were 12-19 years of age and had a family history of pattern hair loss. Regional differences, such as a lower prevalence in Asia and Africa have been reported.^{10,11} Androgenic alopecia-induced hair loss causes severe psychological and emotional distress and impaired quality of life.¹² Current treatment options such as minoxidil and finasteride showed unsatisfactory clinical improvement in some patients.¹³

Autologous platelet-rich plasma (PRP) is prepared from a small volume of the patients' own venous blood (eg, 18 mL) by centrifugation and removal of red blood cells.¹⁴ The result is PRP that contains various growth factors and cytokines released from the granules within platelets.¹⁵ These factors, including platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and insulin-like growth factor-1 (IGF-1), are believed to have various functions which are required for new hair regrowth.¹⁴ PRP is applied by intradermal injections at the affected skin areas and repeated after various intervals.¹⁶ PRP is neither approved in the United States¹⁷ nor in the European Union¹⁸ for hair restoration purposes, though, it may be used in off-label ways. Currently, the evidence to support the clinical efficacy of PRP in pattern hair loss is limited,¹⁹ and its use outside of clinical trials is not recommended.²⁰ This review is important to evaluate the evidence base for the efficacy and the possible adverse events associated with the use of autologous platelet-rich plasma for people with pattern hair loss.

2 | METHODS

While preparing this systematic review, we endorsed the PRISMA statement, adhered to its principles and conformed to its checklist.²¹

2.1 | Inclusion criteria

We included studies with people who have been diagnosed with pattern hair loss by a dermatologist. We considered RCTs with a simple parallel group design and a half-head design. In a half-head design, also called split scalp or split-patch design, different parts of the scalp are randomized to different interventions. The test intervention was autologous platelet-rich plasma (PRP). The comparator was placebo or no treatment. The primary outcome was hair density defined by count of hairs per square centimeter. The secondary outcome was hair diameter expressed in mm. Phototrichogram and global photographs were considered as adequate noninvasive methods to evaluate both hair growth measures.²²

2.2 | Exclusion criteria

We did not consider articles written in other languages than English, and we did not compare various types of PRP preparations or applications.

2.3 | Search strategy

We used search methods as suggested in the Cochrane Handbook for Systematic Reviews of Interventions.²³ We conducted an electronic literature database search without applying any limits in PubMed (US National Library of Medicine) and CENTRAL (Wiley), last search on 24 December 2018. The search strategies are shown in Table 1. We searched for ongoing trials by scanning the online registry ClinicalTrials.gov (US National Library of Medicine) on 24 December 2018 by using the search request "Interventional Studies | Alopecia | platelet rich plasma | Phase 2, 3." We checked the bibliographies of included studies, relevant articles, and review articles for further references to relevant trials. We did not perform a separate search for adverse effects of the target intervention. We wanted to include randomized data only, and thus we did not perform a separate search for adverse effects with respect to other study designs.

2.4 | Data collection and analysis

We imported the bibliographic data into EndNote. Two review authors independently assessed the relevance of imported references, the eligibility of retrieved papers, the risk of bias, and the quality of evidence. We resolved any disagreements by discussion between the two reviewers, no third-party arbitration was necessary. Data were analyzed using the Review Manager software applying random-effects models.²⁴

We included studies reporting on male and/or pattern hair loss or female pattern hair loss only as well as those studies including both types of alopecia. We included all types of PRP, such as

TABLE 1 Search strategies (latest search on 24 December 2018)

Search 1 and 2: MEDLINE via PubMed and CENTRAL via Wiley	
#1	alopecia [MeSH]
#2	androgenetic alopecia
#3	pattern hair loss
#4	baldness
#5	alopecia*
#6	hair loss*
#7	platelet-rich plasma [MeSH]
#8	PRP
#9	platelet-rich* or platelet rich*
#10	#1 or #2 or #3 or #4 or #5 or #6
#11	#7 or #8 or #9
#12	#10 and #11

nonactivated, calcium-activated, or thrombin-activated PRP. We did not include studies with pretreatment or co-treatment with systematic therapy (eg, finasteride, dutasteride, or other antiandrogens) or local therapy (eg, local: minoxidil, prostaglandin, or corticosteroids) compared with placebo. We included the comparisons PRP plus a specific substance vs this substance without PRP, and we assumed a virtual comparison of PRP vs no therapy in those instances. Time point of outcome assessment was 6 months after start of treatment. If this time point was not reported, we accepted another time point within an interval ranging from three to 6 months. Outcomes assessed at time points outside of this interval were not considered in the present review. Predefining time points of interest is highly desirable according to the Methodological Expectations of Cochrane Intervention Reviews (MECIR), because it "guards against selective outcome reporting, and allows users to confirm that choices were not overly influenced by the results".²⁵

Continuous data were analyzed and presented as mean change from baseline provided that the results were measured on the same scale or could be converted to it. We conducted meta-analyses of changes of mean values from baseline by applying the inverse variance method, the random-effects model, and mean difference (changes from baseline) as the effect measure. We pooled data from studies that included males and females, males only and females only. We pooled data from simple parallel and half-head studies. As the difference of means and the respective standard deviation was required for the analyzes, we imputed those values if not reported in the articles. We calculated the mean difference between baseline and 6-month value based on the data extracted from the article. If the respective standard deviations were not provided, then we

imputed standard deviations for changes from baseline from the reported mean values and standard deviations at specific time points according to the Cochrane Handbook Chapter 16.1.3.2 "Imputing standard deviations for changes from baseline".²⁶ If the standard deviations at specific time points were not be reported, then we imputed standard deviations from the reported mean values and the *P* values according the Cochrane Handbook Chapter 7.7.3.3. "Obtaining standard deviations from standard errors, confidence intervals, *t* values, and *P* values for differences in means".²⁷ One study reported the relative standard deviation in percent instead of the standard deviation. According to the Texas A&M University, is "the relative standard deviation expressed in percent and is obtained by multiplying the standard deviation by 100 and dividing this product by the average".²⁸ This formula can be transformed to calculate the standard deviation from a relative standard deviation. The standard deviation is obtained by multiplying the mean by the relative standard deviation and dividing this product by 100. Concerning dichotomous data (eg, weak vs strong subjective improvement, adverse events), we did neither identify valid questionnaires nor serious adverse events. Time-to-event outcomes were not reported in the included studies.

We conformed to Cochrane's principal options for dealing with missing data.²⁹ We sent inquiries by e-mail to ask for clarifying the unit of mean diameter, for mean and standard deviation, and about possible duplicate data, though, we did not receive a reply. We assessed heterogeneity between studies by visual inspection of forest plots and by estimation of the percentage heterogeneity between trials that cannot be ascribed to sampling variation (I^2 statistic).³⁰ An I^2 statistic equal to or greater than 50% was regarded

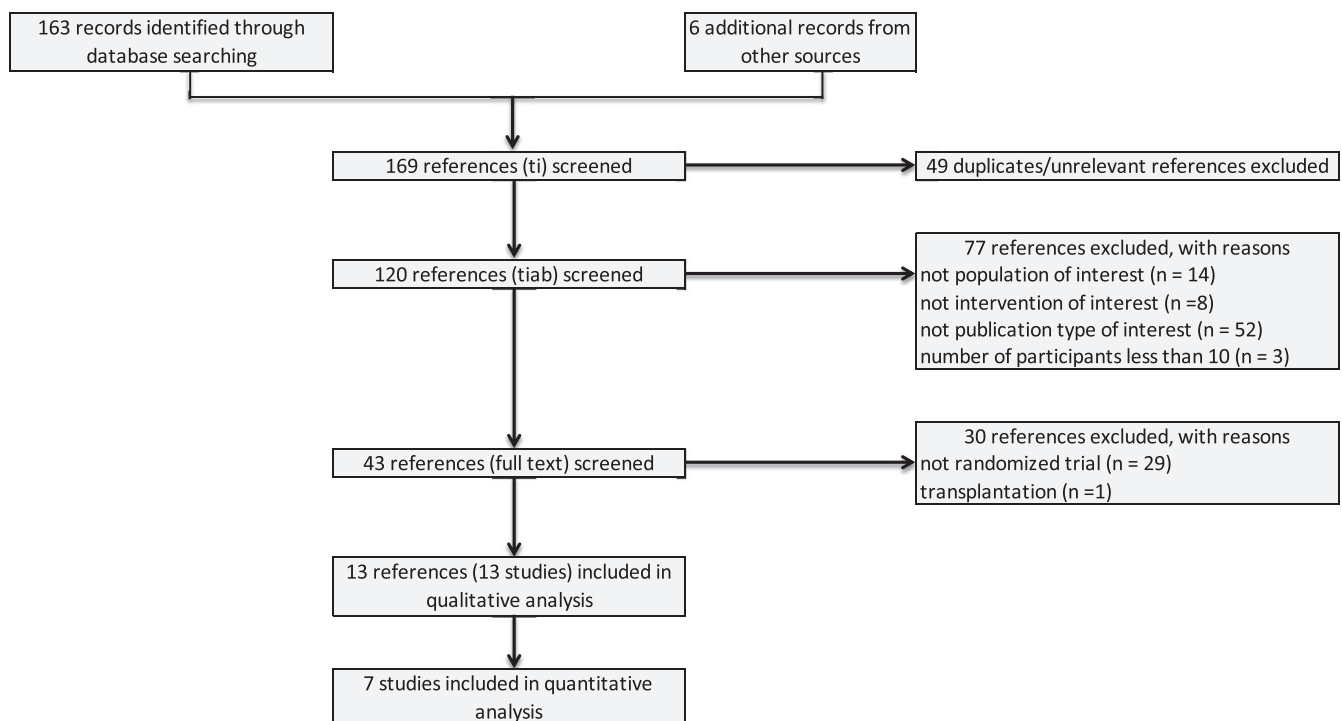


FIGURE 1 Literature search and flow. ti: title; tiab: title and/or abstract

as considerable heterogeneity. We have applied the criteria of The Cochrane Collaboration's tool for assessing risk of bias in RCTs.³¹ We assessed selection bias, performance bias, detection bias, attrition bias, reporting bias, and the possible risk of bias based on co-intervention.

3 | RESULTS

3.1 | Search results

Figure 1 shows the literature retrieval and reference flow. We included 13 RCTs.³²⁻⁴⁴

Among four records retrieved from ClinicalTrials.gov, we identified two potentially relevant ongoing RCTs as follows. A study by the Wake Forest University plans to use a half-head design to compare PRP vs placebo⁴⁵ and a study by the Northwestern University plans to use a crossover design to compare PRP vs placebo.⁴⁶ In searching previous meetings of the American Academy of Dermatology, we identified one poster on a survey inquiring participants on satisfaction and adverse events after receiving PRP to treat pattern hair loss.⁴⁷

3.2 | Baseline data

We provide an overview of the main characteristics of the methods, participants, and interventions of the included studies in Table 2. The 13 included studies randomized 356 participants or half heads, 343 analyzed. Seven studies^{33-39,43} compared scalp patches between two halves of the head and the rest of six studies^{32,38,40-42,44} compared two groups of participants in a simple parallel design. The studies were set in various countries including Brazil, Egypt, India, Italy, Iran, Korea, Mexico, Spain, and the USA. All studies appeared to be conducted in single centers. Six studies included only men,^{35-37,39,41,42} three studies included only women,^{38,40,43} and the rest of four studies included men and women.^{32-34,44} Mean age was roughly 30-45 years ranging from 18 to 63 years. Platelet-rich plasma was applied one to eight times during a treatment period, which lasted from one to 5 months. Three studies applied co-interventions (minoxidil, finasteride, or polydeoxyribonucleotide) in addition to PRP in the experimental group and applied the same intervention in the control group without PRP.^{34,38,42} The rest of 10 studies compared platelet-rich plasma to placebo (normal saline or distilled water).^{32,33,35-37,39-41,43,44} If studies included males, then the studies used the Hamilton-Norwood classification to categorize progression of male pattern hair loss. If studies included females, then the studies applied the Ludwig classification to categorize progression of female pattern hair loss. Evaluation of hair density and hair diameter was performed by global photography and phototrichogram.

3.3 | Risk of bias

We provide a summary of the risk of bias assessment in Figure 2. In five studies,^{32,34,38,41,42} the assessment resulted in the judgement

of a high risk in at least one item. In one of those five studies,³⁴ the high risk was supported by two different types of co-interventions, though a single type of co-intervention was applied to a single person in the experimental as well as in the control group. In the rest of eight studies, we did not judge a high risk of bias. Adequate sequence generation was judged in three studies and adequate allocation concealment in two studies. Adequate reporting of blinding of participants and personnel was judged in five studies and outcome assessment in nine studies. Except in two studies, the studies reported either little or no dropouts. We did not identify obvious selective outcome reporting. Nevertheless, we were not completely convinced about absence of this type of bias in any study. We did not judge a high risk of bias in any of the studies that were included in the meta-analysis on hair density.

3.4 | Outcomes

We provide an overview of the outcomes and time point of assessment in Table 3. Data of seven studies on the outcome hair density were included in the meta-analysis.^{33,34,36,37,39,43,44} One of those seven studies compared PRP plus minoxidil or finasteride vs placebo plus minoxidil or finasteride accordingly.³⁴ Five studies assessed this outcome at 6 months after start of intervention,^{33,34,39,43,44} and the rest of two studies at 3 months.^{36,37} The forest plot in Figure 2 shows that the study data favored PRP on increasing hair density in males and females when compared to placebo with a pooled mean difference of 30.35 (95% confidence interval 1.77-58.93) and a *P* value of less than 0.00001. Five of those seven studies reported statistically significant results in favor of PRP.^{34,36,37,43,44} Difference of data between the groups of the rest of two studies was not statistically significant and did not favor any treatment group.^{33,39} The heterogeneity did not appear to be related to number, age or gender of participants, study design, type of co-intervention, or type of comparator. We did not conduct a meta-analysis of the secondary outcome hair diameter because only a single study was eligible for inclusion.⁴³ The data of this study favored PRP when compared to placebo.

4 | DISCUSSION

4.1 | Overall completeness and applicability of evidence

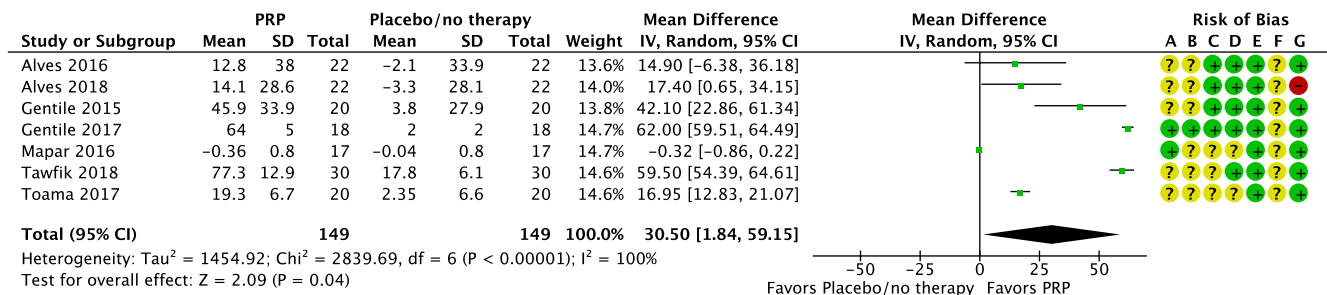
Ten studies reported the primary outcome hair density, of which seven were included in the meta-analysis. Cervelli et al³⁵ included data of ten participants, which were again included by Gentile et al.³⁶ We considered these data only once, because duplicate data would bias the pooled estimate in one direction. Thus, the quantitative analysis included the data reported by Gentile et al³⁶ but not those by.³⁵ Two other studies^{40,41} did not report absolute density data.

None of the studies included in the meta-analysis of the primary outcome hair density reported the standard deviation of the mean change from baseline. To complement this measure of the

TABLE 2 Characteristics of methods, participants, and interventions

Study ID	Design; Country; Blinding	Participants	Intervention	Comparator	Comment
Abaroa 2016 ²⁵	Simple parallel; recruited in Mexico; blinding: Part/Invest/OA	(R)/A: (20)/20; I vs C: 17 vs 3; M/F: 11/3 vs 6/0; age: mean 44.2 vs 31.7, range 24-54 vs 22-47 y; HN:nr; L:nr	8× PRP at 3-dy interval in 3 wk; no co-intervention	Placebo (distilled water)	Group sizes differ
Alves 2016 ²⁶	Half head; recruited Jan 2014 to Nov 2014 in Spain; blinding: Part/OA	(R)/A: (25)/22; M/F: 11/11; age: mean 39, range 21-62 y; HN:II-V; L:I-III	3× PRP at 1-mo interval within 2 mo; no co-intervention	Placebo (normal saline)	None
Alves 2018 ²⁷	Half head; recruited in Spain; blinding: Part/OA (Alves 2016)	(R)/A: (25)/24; M/F: 11/13; age: mean 39.9, range 18-65 y; HN:II-V; L:I-III (Alves 2016)	3× PRP at 1-mo interval in 2 mo plus topical minoxidil (n = 13) twice daily or plus oral finasteride (n = 11) daily	Placebo plus minoxidil or finasteride accordingly	Co-intervention
Cervelli 2014 ²⁸	Half head; recruited in Italy; blinding: OA	(R)/A: (10)/10; M/F: 10/0; age: range 20-52 y; HN:IIa-IV	3× PRP at 1-mo interval in 2 mo; no co-intervention	Placebo (normal saline)	Male only; included in Gentile 2015
Gentile 2015 ²⁹	Half head; recruited in Italy; blinding: OA	(R)/A: (23)/20; M/F: 20/0; age: range 19-63 y; HN:IIa-IV	3× PRP at 1-mo interval in 2 mo; no co-intervention	Placebo (normal saline)	Male only
Gentile 2017 ³⁰	Half head; Italy; blinding: Part/Invest/OA	(R)/A: (18)/18; M/F: 18/0; age: range 19-63 y; HN:II-IV	3× nonactivated PRP at 1-mo interval in 2 mo; no co-intervention	Placebo (normal saline)	Male only
Lee 2015 ³¹	Simple parallel; recruited in Korea; blinding: OA	(R)/A: (40)/40; I vs C: 20 vs 20; M/F: 0/20 vs 0/20; age: mean 35.4 vs 32.5, range 20-60 vs 23-43 y; L:nr	1× PRP plus 12× PDRN at 1-wk interval	12× PDRN at weekly intervals	Female only; co-intervention
Mapar 2016 ³²	Half head; recruited Jul 2013 to Jul 2014 in Iran; blinding: OA	(R)/A: (19)/17; M/F: 17/0; age: range 25-45 y; HN:IV-VI	2× PRP at 1-mo interval in 1 mo; no co-intervention	Placebo (normal saline)	Male only
Puig 2016 ³³	Simple parallel; recruited in USA; blinding: Part/OA	(R)/A: (26)/26; I vs C: 15 vs 11; M/F: 0/15 vs 0/11; age: range ≥18 y; L:II	1× PRP at BL; no co-intervention	Placebo (normal saline)	Female only
Rodriguez 2018 ³⁴	Simple parallel; recruited Aug 2014 to Oct 2016 in Brazil; no blinding	(R)/A: (30)/26; I vs C: 15 vs 11; M/F: 15/0 vs 11/0; age: median (± SD) 32 (± 7.2) years; HN:III	4× PRP at 0.5-mo interval in 1.5 mo; no co-intervention	Placebo (normal saline)	Male only
Shah 2017 ³⁵	Simple parallel; India; no blinding	(R)/A: (50)/50; I vs C: 25 vs 25; M/F: 25/0 vs 25/0; age: mean 30.6, range 18-50 y; HN:III-V	6× PRP at 1-mo interval in 5 mo plus topical minoxidil twice daily	Topical minoxidil twice daily	Male only; co-intervention
Tawfik 2018 ³⁶	Half head; recruited in Egypt; blinding: Part/OA	(R)/A: (30)/30; M/F: 0/30; age: mean 29.3, range 20-45 y; L:III	4× PRP at 1-wk interval in 1 mo; no co-intervention	Placebo (normal saline)	Female only
Toama 2017 ³⁷	Simple parallel; recruited May 2014 to Apr 2015 in Egypt; no blinding	(R)/A: (40)/40; I vs C: 20 vs 20; M/F: 11/9 vs 8/12; age: mean 28.5 vs 28.8, range 18-45 y vs 19-40; HN:I-V; L:I-III	5× PRP at 2-wk interval in 2 mo; no co-intervention	Placebo (normal saline)	None

Note: Simple parallel: design according to The Cochrane Handbook section 9.3.1, quote: "participants are individually randomized to one of two intervention groups, and a single measurement for each outcome from each participant is collected and analyzed." Half head: design according to The Cochrane Handbook section 9.3.1, quote: "multiple observations for the same outcome," such as repeated measurements on different body parts, specifically comparing a part of the right side of the scalp to a part of left side of the scalp. Abbreviations: (R)/A, number of (randomized)/analyzed participants; BL, baseline; HN, Hamilton-Norwood classification of male hair loss pattern; I vs C, intervention vs comparator group; Invest, investigator, study personnel, nurses, physicians; L, Ludwig classification of female hair loss pattern; M/F, number of male/female participants; mo, month(s); OA, outcome assessment; Part, participants; PDRN, polydeoxyribonucleotide; PRP, platelet-rich plasma; SD, standard deviation; T/O, topical/oral; wk, weeks.



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Co-intervention

FIGURE 2 Meta-analysis hair density. Forest plot of the change of mean hair density at three to 6 mo from baseline after treatment with platelet-rich plasma (PRP). Alves 2018³⁴ compared PRP plus minoxidil or finasteride accordingly vs placebo plus minoxidil or finasteride accordingly. The rest of six studies^{33,36,37,39,43,44} compared PRP vs placebo (normal saline)

spread of values in a distribution, which is required for inclusion in the meta-analysis, we applied methods of imputations by use of a correlation coefficient and by use of the *P* value. Although we implemented the recommendations published by the Cochrane Handbook, we may have introduced bias concomitantly. Imputation means that we did not use actual study data, but rather used an estimate based on certain conditions. The real but unknown values might differ from those estimates distinctly. We e-mailed the respective authors to request the missing values but did not receive the data.

Three studies reported the outcome hair diameter. One study⁴³ reported mean values and standard deviations at the specific times points baseline and 6 months. We were able to calculate the mean change from baseline, but the reported data were not sufficient to calculate the respective standard deviation. We used an imputation method to estimate the missing value, which allowed us to include the respective data in the analysis. Regarding two studies,^{38,44} we were unsure about the unit of the reported values. We e-mailed the authors to request the missing values but did not receive the data. Thus, these studies were not included in the analysis. Furthermore, one of those studies³⁸ reported \pm percent instead of \pm standard deviation. Although, the authors reported mean change from baseline, we would like to remind that percentage change from baseline should not be used in statistical analysis, because percentage change from baseline may fail to protect from bias in the case of baseline imbalance.⁴⁸

4.2 | Agreements and disagreements with other studies or reviews

Chen et al⁴⁹ included eight RCTs and 16 prospective cohort studies. We also included seven of these eight RCTs. One other RCT investigated PRP vs minoxidil, a comparison which did not match the inclusion criteria of the present review. Thus, we included six additional RCTs not considered by Chen et al.⁴⁹ Chen et al⁴⁹ did not

mention that Gentile et al³⁶ reported the identical data reported by Cervelli et al³⁵ on 10 people, though this introduced duplicate data bias in favor of PRP. Chen et al⁴⁹ concluded that PRP is a favorable low-risk intervention for pattern hair loss. In concordance with the present review, the authors identified objective improvement of hair density and no serious complications. The authors also suggested a good patient satisfaction. In RCTs, we did not find sufficient data on health-related quality of life, likely because we did not include cohort studies.

4.3 | Strengths and limitations

The present review was based on a comprehensive search, and we provided detailed study characteristics including extended support for judgements of the risk of bias assessment. Of 13 studies considered in the qualitative analysis, we included seven studies in the quantitative analysis of the primary outcome hair density. In the rest of five studies, this outcome was not reported or data could not be used due to low quality reporting. We found duplicate data and excluded those data from the analysis. We applied imputation methods to provide for standard deviation values on mean change from baseline. There is a potential that this approach could have introduced bias, though it does not appear probable that the direction of the pooled estimate could be changed by this potential bias. We assumed the virtual comparison PRP vs no therapy, whereas, in reality, PRP plus standard therapy was compared with the same standard therapy only. However, the results could be different from a real comparison PRP vs no therapy without co-intervention. There could be an interactive effect instead of just an additive effect. We did not compare PRP vs other active treatments. There is considerable heterogeneity among the study data included in the meta-analysis. We performed a random-effects meta-analysis to account for heterogeneity that cannot be explained. Nevertheless, it may be misleading to quote an average value for the intervention effect.⁵⁰

TABLE 3 Results

Study ID	Outcome	Intervention	Comparator	Change from BL (I vs C)	Statistics I vs C	Comment	MA
Abaroa 2016 ²⁵	Follicle count, number, median (range) at 3 mo vs BL	5 (2-11) vs 4 (1-11)	3 (3-3) vs 7 (4-9)	1 vs -4	Not reported	Not predefined outcome	-
Abaroa 2016 ²⁵	Follicle diameter, mm, mean (range) at 3 mo vs BL	0.3 (0.1-0.8) vs 0.3 (0.1-0.9)	0.8 (0.2-1.0) vs 0.8 (0.5-0.8)	1 vs -4	Not reported	Not predefined outcome	-
Alves 2016 ²⁶	Density: 1/cm ² , mean (\pm SD) at 6 mo vs BL	179.9 (\pm 62.7) vs 167.1 (\pm 55.6)	165.7 (\pm 55.2) vs 167.8 (\pm 51.2)	12.8 (\pm 38.0) vs -2.1 (\pm 33.9)	P < .05	SD imputed by correction coefficient; P not correct	Yes
Alves 2018 ²⁷	Density: 1/cm ² , mean (\pm SD) at 6 mo vs BL	163.6 (\pm 47.1) vs 149.5 (\pm 42)	147.5 (\pm 41.6) vs 150.8 (\pm 46.1)	14.1 (28.6) vs -3.3 (28.1)	P < .05	SD imputed by correction coefficient	Yes
Cervelli 2014 ²⁸	Density: 1/cm ² , mean (\pm SD) at 3 mo vs BL	187.1 \pm 52.5 vs 159.4 \pm 47.6	168.1 \pm 43.3 vs 171.2 \pm 44.4	27.7 (32.0) vs -3.1 (27.8)	P < .0001	SD imputed by correction coefficient	-
Gentile 2015 ²⁹	Density: 1/cm ² , mean (\pm SD) at 3 mo vs BL	207.1 (\pm 56.3) vs 161.2 (\pm 41.9)	170.3 (\pm 42.1) vs 166.5 (\pm 45.6)	45.9 (\pm 33.9) vs 3.8 (\pm 27.9)	P < .0001	SD imputed by correction coefficient	Yes
Gentile 2017 ³⁰	Density: 1/cm ² , mean (\pm SD) at 3 mo vs BL	282 (\pm 20) vs 218 (\pm 17)	227 (\pm 16) vs 225 (\pm 15)	64 (\pm 5) vs 2 (\pm 2)	Not reported	P value not provided	Yes
Lee 2015 ³¹	Diameter: mean change from BL (\pm SD) at 3 mo	Not reported	Not reported	16.8 (\pm 10.8%) vs 13.5 (\pm 10.7%)	P = .031	Unit of mean hair diameter not reported	-
Mapar 2016 ³²	Density (terminal hair): 1/cm ² , mean (\pm SD) at 6 mo vs BL	13.61 vs 13.97	14.68 vs 14.72	-0.36 (\pm 0.8) vs -0.04 (\pm 0.8)	P = .25	SD imputed from P value	Yes
Puig 2016 ³³	Density: 1/cm ² , mean (\pm SD) at 6 mo vs BL	Not reported	Not reported	Not reported	P = .503	Hair check data box area 4 cm ²	-
Rodriguez 2018 ³⁴	Density: 1/cm ² , mean (\pm SD) at 6 mo vs BL	Not reported	Not reported	Not reported	Not reported	Lack of reported data	-
Shah 2017 ³⁵	Patient's 4-point scales (0 to +3) at 6 mo	Not reported	Not reported	Moderate or excellent improvement: 23/25 vs 12/25	P < .05	Not validated questionnaire	-
Tawfik 2018 ³⁶	Density: 1/cm ² , mean (\pm SD) at 6 mo vs BL	150.94 (\pm 19.17) vs 73.66 (\pm 9.42)	91.06 (\pm 9.06) vs 73.25 (\pm 9.98)	77.3 (\pm 12.9) vs 17.8 (\pm 6.1)	P < .005	SD imputed by correction coefficient	Yes
Tawfik 2018 ³⁶	Diameter: mm, mean change from BL (\pm SD) at 6 mo	0.21 (\pm 0.04) vs 0.1 (\pm 0.03)	0.13 (\pm 0.03) vs 0.1 (\pm 0.03)	0.11 (\pm 0.024) vs 0.03 (\pm 0.019)	P < .005	SD imputed by correction coefficient	-
Toama 2017 ³⁷	Density: 1/cm ² , mean (\pm SD) at 6 mo vs BL	56.65 (\pm 10.99) vs 37.35 (\pm 7.49)	46.55 (\pm 10.27) vs 44.2 (\pm 5.87)	19.3 (\pm 6.7) vs 2.4 (\pm 6.6)	Not reported	SD imputed by correction coefficient	Yes
Toama 2017 ³⁷	Diameter: mm/10 000, mean (\pm SD) at 6 mo vs BL	10.97 (\pm 2.98) vs 5.24 (\pm 1.63)	7.34 (\pm 2.26) vs 7.22 (\pm 2.43)	5.73 (\pm 116.9) vs 0.12 (\pm 1.5)	Not reported	Invalid unit	-

Note: Imputed number typed in italic. BL: baseline; MA: meta-analysis. Mapar 2016³⁹ reported number of hairs counted in 2.5 times 2.5 cm². These squares have an area of 6.25 cm². We divided the values given by 6.25 to attain the unit of density of 1/cm².

4.4 | Outlook

We recommend further RCTs that should ensure adequate random sequence generation, adequate allocation concealment, blinding of performance and detection, and that should prevent incomplete data and selective reporting. Regarding the time point at outcome assessment, we think that the phrase “end of treatment” does not appear adequate and should be specified. To consider any potential harm by PRP, future study protocols might include long-term observations. It seems meaningful to create and update a valid questionnaire on health-related quality of life that can also be appropriate for use in RCTs. Future studies should clarify the reporting and should conform to the CONSORT statement.⁵¹ Rodrigues 2018 did not identify an association between an increase in the hair density within the PRP group and the levels of platelet count, platelet-derived growth factor, epidermal growth factor, and vascular endothelial growth factor.⁴¹ These results suggest other mechanisms to be involved in the process.

5 | CONCLUSIONS

The pooled results of seven RCTs indicated that autologous platelet-rich plasma could increase hair density in males and females when compared to placebo or no treatment. We did not identify serious short-term treatment-related adverse events.

ORCID

Haibo Liu  <https://orcid.org/0000-0001-7705-2202>

Sandra Peternel  <https://orcid.org/0000-0001-8590-0451>

Alexander Labeit  <https://orcid.org/0000-0002-4709-4767>

Frank Peinemann  <https://orcid.org/0000-0002-4727-1313>

REFERENCES

- Vary JC Jr. Selected disorders of skin appendages-acne, alopecia, hyperhidrosis. *Med Clin North Am.* 2015;99(6):1195-1211.
- Olsen EA. Androgenetic alopecia. In: Olsen EA, ed. *Disorders of Hair Growth.* New York, NY: McGraw-Hill; 1994:257-283.
- Hamilton JB. Patterned loss of hair in man; types and incidence. *Ann N Y Acad Sci.* 1951;53:708-728.
- Gupta M, Mysore V. Classifications of patterned hair loss: a review. *J Cutan Aesthet Surg.* 2016;9(1):3-12.
- Norwood OT. Male pattern baldness: classification and incidence. *South Med J.* 1975;68:1359-1365.
- Piraccini BM, Alessandrini A. Androgenetic alopecia. *G Ital Dermatol Venereol.* 2014;149(1):15-24.
- Norwood OT. Incidence of female androgenetic alopecia (female pattern alopecia). *Dermatol Surg.* 2001;27:53-54.
- Ludwig E. Classification of the types of androgenetic alopecia (common baldness) occurring in the female sex. *Br J Dermatol.* 1977;97:247-254.
- Gonzalez ME, Cantatore-Francis J, Orlov SJ. Androgenetic alopecia in the pediatric population: a retrospective review of 57 patients. *Br J Dermatol.* 2010;163:378-385.
- Khumalo NP, Jessop S, Gumedze F, Ehrlich R. Hairdressing and the prevalence of scalp disease in African adults. *Br J Dermatol.* 2007;157:981-988.
- Paik J-H, Yoon J-B, Sim W-Y, Kim B-S, Kim N-I. The prevalence and types of androgenetic alopecia in Korean men and women. *Br J Dermatol.* 2001;145:95-99.
- Alfonso M, Richter-Appelt H, Tosti A, Viera MS, Garcia M. The psychosocial impact of hair loss among men: a multinational European study. *Curr Med Res Opin.* 2005;21(11):1829-1836.
- Stevens J, Khetarpal S. Platelet-rich plasma for androgenetic alopecia: A review of the literature and proposed treatment protocol. *Int J Womens Dermatol.* 2018;5(1):46-51.
- Alves R, Grimalt R. A review of platelet-rich plasma: history, biology, mechanism of action, and classification. *Skin Appendage Disord.* 2018;4(1):18-24.
- Blair P, Flaumenhaft R. Platelet alpha-granules: basic biology and clinical correlates. *Blood Rev.* 2009;23:177-189.
- Motosko CC, Khouri KS, Poudrier G, Sinno S, Hazen A. Evaluating platelet-rich therapy for facial aesthetics and alopecia: a critical review of the literature. *Plast Reconstr Surg.* 2018;141(5):1115-1123.
- Beitzel K, Allen D, Apostolakis J, et al. US definitions, current use, and FDA stance on use of platelet-rich plasma in sports medicine. *J Knee Surg.* 2015;28:29-34.
- EDQM. *Guide to the quality and safety of tissues and cells for human application*, 3rd ed. Strasbourg: European Directorate for the Quality of Medicines & HealthCare (EDQM), Council of Europe, 2017. <https://register.edqm.eu/freepub>. Accessed June 14, 2019.
- Leo MS, Kumar AS, Kirit R, Konathan R, Sivamani RK. Systematic review of the use of platelet-rich plasma in aesthetic dermatology. *J Cosmet Dermatol.* 2015;14(4):315-323.
- BAeK. *Querschnitts-Leitlinien (BÄK) zur Therapie mit Blutkomponenten und Plasmaderivaten*, 4. überarbeitete und aktualisierte Auflage 2014. Berlin: Bundesärztekammer, 2014. https://www.bundesaerztekammer.de/fileadmin/user_upload/downloads/QLL_Haemo_therapie_2014.pdf. Accessed June 14, 2019.
- Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Medicine.* 2009;6:e1000097.
- Dhurat R, Saraogi P. Hair evaluation methods: merits and demerits. *Int J Trichology.* 2009;1(2):108-119.
- Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins J, Green S (eds.). *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011)*. London: Cochrane, 2011. https://handbook-5-1.cochrane.org/chapter_6/6_searching_for_studies.htm. Accessed December 30, 2018.
- Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre; 2014.
- Higgins J, Lasserson T, Chandler J, Tovey D, Churchill R. Methodological Expectations of Cochrane Intervention Reviews. Version 1.06. London: Cochrane, 2018. <https://community.cochrane.org/mecir-manual/standards-conduct-new-cochrane-intervention-reviews-c1-75/developing-protocol-review-c1-23/selecting-outcomes-be-addressed-studies-included-review-c14-18>. Accessed June 14, 2019.
- Higgins J, Deeks JJ, Altman DG, eds. Chapter 16: Special topics in statistics. In: Higgins J, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011)*. London: Cochrane; 2011. https://handbook-5-1.cochrane.org/chapter_16/16_1_3_2_imputing_standard_deviations_for_changes_from_baseline.htm. Accessed June 14, 2019.
- Higgins J, Deeks JJ, eds. Chapter 7: Selecting studies and collecting data. In: Higgins J, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011)*. London: Cochrane; 2011. <https://handbook-5-1.cochrane.org/>

- chapter_7/7_7_3_3_obtaining_standard_deviations_from_standard_errors.htm. Accessed June 14, 2019.
28. TAMU. Average, Standard Deviation and Relative Standard Deviation. College Station: Department of Chemistry, Texas A&M University. <http://www.chem.tamu.edu/class/fyp/keeney/stddev.pdf>. Accessed 30 December 2018.
 29. Higgins J, Deeks JJ, Altman DG, eds. Chapter 16: Special topics in statistics. In: Higgins J, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* (updated March 2011). London: Cochrane; 2011. https://handbook-5-1.cochrane.org/chapter_16/16_1_2_general_principles_for_dealing_with_missing_data.htm. Accessed June 14, 2019.
 30. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327(7414):557-560.
 31. Higgins J, Altman DG, Sterne J, eds. Chapter 8: Assessing risk of bias in included studies. In: Higgins J, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* (updated March 2011). London: Cochrane; 2011. https://handbook-5-1.cochrane.org/chapter_8/table_8_5_d_criteria_for_judging_risk_of_bias_in_the_risk_of.htm. Accessed June 14, 2019.
 32. Abaroa F, Reyes K, Barrera D, et al. Histological findings of follicular units in patients with androgenetic alopecia before and after application of autologous platelet-rich plasma. *Dermatologia Rev Mex*. 2016;60(2):97-105.
 33. Alves R, Grimalt R. Randomized placebo-controlled, double-blind, half-head study to assess the efficacy of platelet-rich plasma on the treatment of androgenetic alopecia. *Dermatol Surg*. 2016;42(4):491-497.
 34. Alves R, Grimalt R. Platelet-rich plasma in combination with 5% minoxidil topical solution and 1 mg oral finasteride for the treatment of androgenetic alopecia: a randomized placebo-controlled, double-blind, half-head study. *Dermatol Surg*. 2018;44(1):126-130.
 35. Cervelli V, Garcovich S, Bielli A, et al. The effect of autologous activated platelet rich plasma (AA-PRP) injection on pattern hair loss: clinical and histomorphometric evaluation. *Biomed Res Int*. 2014;2014:760709.
 36. Gentile P, Garcovich S, Bielli A, Scioli MG, Orlandi A, Cervelli V. The effect of platelet-rich plasma in hair regrowth: a randomized placebo-controlled trial. *Stem Cells Transl Med*. 2015;4(11):1317-1323.
 37. Gentile P, Cole J, Cole M, et al. Evaluation of not-activated and activated PRP in hair loss treatment: role of growth factor and cytokine concentrations obtained by different collection systems. *Int J Mol Sci*. 2017;18(2):408.
 38. Lee SH, Zheng Z, Kang JS, Kim DY, Oh SH, Cho SB. Therapeutic efficacy of autologous platelet-rich plasma and polydeoxyribonucleotide on female pattern hair loss. *Wound Repair Regen*. 2015;23(1):30-36.
 39. Mapar MA, Shahriari S, Haghhighizadeh MH. Efficacy of platelet-rich plasma in the treatment of androgenetic (male-patterned) alopecia: a pilot randomized controlled trial. *J Cosmet Laser Ther*. 2016;18(8):452-455.
 40. Puig CJ, Reese R, Peters M. Double-blind, placebo-controlled pilot study on the use of platelet-rich plasma in women with female androgenetic alopecia. *Dermatol Surg*. 2016;42(11):1243-1247.
 41. Rodrigues BL, Montalvão S, Cancela R, et al. Treatment of male pattern alopecia with platelet-rich plasma: a double-blind controlled study with analysis of platelet number and growth factor levels. *J Am Acad Dermatol*. 2019;80(3):694-700.
 42. Shah KB, Shah AN, Solanki RB, Raval RC. A comparative study of microneedling with platelet-rich plasma plus topical minoxidil (5%) and topical minoxidil (5%) alone in androgenetic alopecia. *Int J Trichology*. 2017;9(1):14-18.
 43. Tawfik AA, Osman M. The effect of autologous activated platelet-rich plasma injection on female pattern hair loss: a randomized placebo-controlled study. *J Cosmet Dermatol*. 2018;17(1):47-53.
 44. Toama M, Soliman I. Platelet rich plasma treatment of androgenetic alopecia in men and women. *J Clin Investig Dermatol*. 2017;5(2):5.
 45. ClinicalTrials.gov: NCT03474718. *Evaluating the Efficacy of Platelet-Rich Plasma Therapy in the Treatment of Androgenic Alopecia*. Bethesda: National Library of Medicine; 2018.
 46. ClinicalTrials.gov: NCT03048461. *The Effect of Platelet-Rich Plasma in Subjects with Androgenetic Alopecia*. Bethesda: National Library of Medicine; 2018.
 47. Laird M, Lo-Sicco KI, Reed ML, Brinster NK. [5258] Platelet-rich plasma for the treatment of androgenetic alopecia: a patient survey. *J Am Acad Dermatol*. 2017;76(6 Suppl 1):AB199.
 48. Vickers AJ. The use of percentage change from baseline as an outcome in a controlled trial is statistically inefficient: a simulation study. *BMC Med Res Methodol*. 2001;1:6.
 49. Chen JX, Justicz N, Lee LN. Platelet-rich plasma for the treatment of androgenic alopecia: a systematic review. *Facial Plast Surg*. 2018;34(6):631-640.
 50. Deeks JJ, Higgins J, Altman DG, eds. Chapter 9: Analysing data and undertaking meta-analyses. In: Higgins J, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* (updated March 2011). London: Cochrane; 2011. https://handbook-5-1.cochrane.org/chapter_9/9_5_3_strategies_for_addressing_heterogeneity.htm. Accessed June 14, 2019.
 51. Schulz KF, Altman DG, Moher D, CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *PLoS Medicine*. 2010;7(3):e1000251.

How to cite this article: Dervishi G, Liu H, Peternel S, Labeit A, Peinemann F. Autologous platelet-rich plasma therapy for pattern hair loss: A systematic review. *J Cosmet Dermatol*. 2020;19:827-835. <https://doi.org/10.1111/jocd.13113>

Copyright of Journal of Cosmetic Dermatology is the property of Wiley-Blackwell and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.