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

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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

[Correction added on 19 November 2020, after first online publication: Projekt Deal funding statement has been added.]

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 States[17] nor in the European Union[18] 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 are 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

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

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 non-activated, 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-analyzes 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

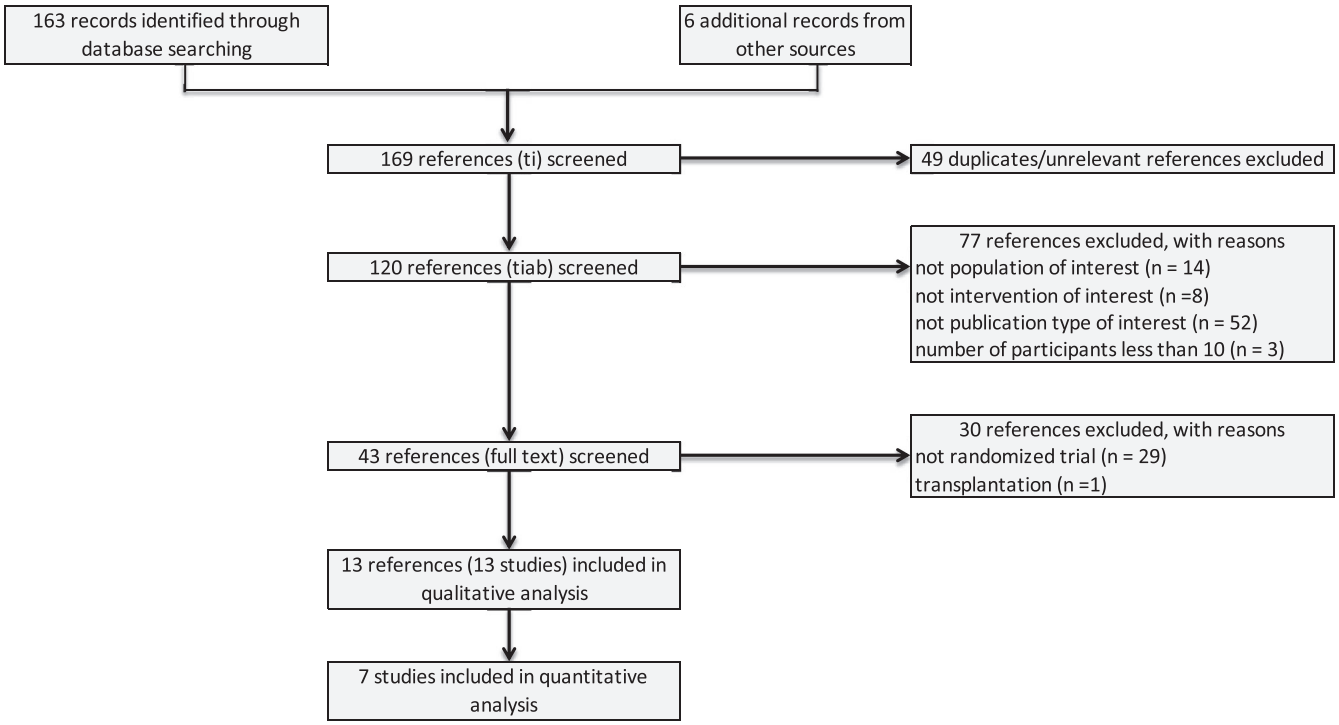

FIGURE 1 Literature search and flow. ti: title; tiab: title and/or abstract

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 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 placebo[45] 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 al[35] 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 al[36] but not those by.[35] Two other studies[40,41] did not report absolute density data.

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:I-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–II	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 deviaion; T/O, topical/oral; wk, weeks.

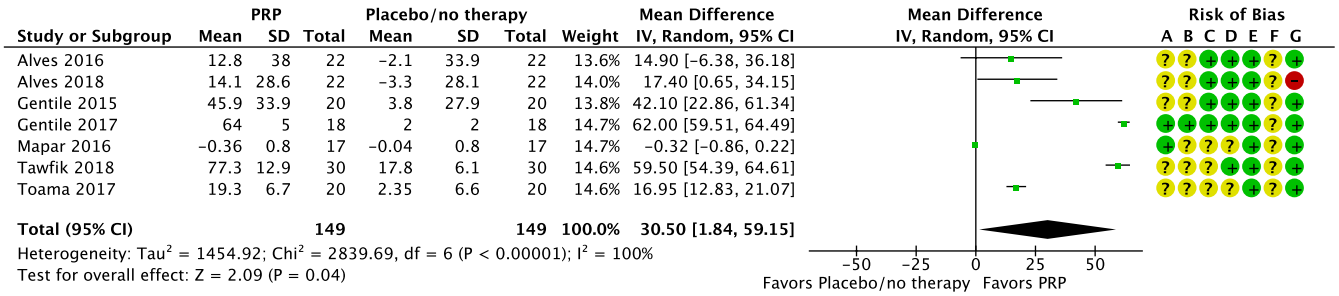

FIGURE 2 Meta-analysis hair density. Forest plot of the change of mean hair density at three to 6 mo from baseline after treatment with platelet-rich plasma (PRP). Alves 2018[34] compared PRP plus minoxidil or finasteride accordingly vs placebo plus minoxidil or finasteride accordingly. The rest of six studies[33,36,37,39,43,44] compared PRP vs placebo (normal saline)

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 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 study[43] 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 studies[38] reported ± percent instead of ± 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 al[49] 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 al[49] did not mention that Gentile et al[36] reported the identical data reported by Cervelli et al[35] on 10 people, though this introduced duplicate data bias in favor of PRP. Chen et al[49] 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

TABLE 3 Results

Study ID	Outome	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 (±SD) at 6 mo vs BL	179.9 (±62.7) vs 167.1 (±55.6)	165.7 (±55.2) vs 167.8 (±51.2)	12.8 *(±38.0)* vs −2.1 *(±33.9)*	$P < .05$	SD imputed by correction coefficient; P not correct	Yes
Alves 2018[27]	Density: 1/cm^2, mean (±SD) at 6 mo vs BL	163.6 (±47.1) vs 149.5 (±42)	147.5 (±41.6) vs 150.8 (±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 (±SD) at 3 mo vs BL	187.1 ± 52.5 vs 159.4 ± 47.6	168.1 ± 43.3 vs 171.2 ± 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 (±SD) at 3 mo vs BL	207.1 (±56.3) vs 161.2 (±41.9)	170.3 (±42.1) vs 166.5 (±45.6)	45.9 *(±33.9)* vs 3.8 *(±27.9)*	$P < .0001$	SD imputed by correction coefficient	Yes
Gentile 2017[30]	Density: 1/cm^2, mean (±SD) at 3 mo vs BL	282 (±20) vs 218 (±17)	227 (± 16) vs 225 (± 15)	64 (±5) vs 2 (±2)	Not reported	P value not provided	Yes
Lee 2015[31]	Diameter: mean change from BL (±SD) at 3 mo	Not reported	Not reported	16.8 (±10.8%) vs 13.5 (±10.7%)	$P = .031$	Unit of mean hair diameter not reported	–
Mapar 2016[32]	Density (terminal hair): 1/cm^2, mean (±SD) at 6 mo vs BL	13.61 vs 13.97	14.68 vs 14.72	-0.36 *(±0.8)* vs −0.04 *(±0.8)*	$P = .25$	SD imputed from P value	Yes
Puig 2016[33]	Density: 1/cm^2, mean (±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 (±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 (±SD) at 6 mo vs BL	150.94 (±19.17) vs 73.66 (±9.42)	91.06 (±9.06) vs 73.25 (±9.98)	77.3 *(±12.9)* vs 17.8 *(±6.1)*	$P < .005$	SD imputed by correction coefficient	Yes
Tawfik 2018[36]	Diameter: mm, mean change from BL (±SD) at 6 mo	0.21 (±0.04) vs 0.1 (±0.03)	0.13 (±0.03) vs 0.1 (±0.03)	0.11 *(±0.024)* vs 0.03 *(±0.019)*	$P < .005$	SD imputed by correction coefficient	–
Toama 2017[37]	Density: 1/cm^2, mean (±SD) at 6 mo vs BL	56.65 (±10.99) vs 37.35 (±7.49)	46.55 (±10.27) vs 44.2 (±5.87)	19.3 *(±6.7)* vs 2.4 *(±6.6)*	Not reported	SD imputed by correction coefficient	Yes
Toama 2017[37]	Diameter: mm/10 000, mean (±SD) at 6 mo vs BL	10.97 (±2.98) vs 5.24 (±1.63)	7.34 (±2.26) vs 7.22 (±2.43)	5.73 *(±116.9)* vs 0.12 *(±1.5)*	Not reported	Invalid unit	–

Note: Imputed number typed in italic. BL: baseline; MA: meta-analysis. Mapar 2016[39] reported number of hairs counted in 2.5 times 2.5 cm^2. These squares have an area of 6.25 cm^2. We divided the values given by 6.25 to attain the unit of density of 1/cm^2.

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]

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.

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