Review / Derleme

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Intrauterine infusion and sub-endometrial injection of autologous platelet-rich plasma for thin endometrium: A systematic review and single-arm meta-analysis

İnce endometriumda otolog trombositten zengin plazmanın rahim içi infüzyonu ve subendometrial enjeksiyonu: Sistematik bir derleme ve tek kollu meta-analiz

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Abstract

To evaluate the efficacy and safety of autologous platelet-rich plasma (PRP), administered via intrauterine infusion or subendometrial injection, for improving endometrial thickness (EMT) and pregnancy outcomes in women with thin endometrium undergoing frozen-thawed embryo transfer (FET) cycles. A comprehensive literature search was conducted across PubMed, Embase, Web of Science, and the Cochrane Library in accordance with preferred reporting items for systematic reviews and meta-analyses recommendations. Eligible studies investigating PRP treatment for thin endometrium in FET cycles were included. Methodological quality was assessed using the Methodological Index for Non-Randomized Studies. Pooled mean differences (MD) for EMT and aggregated proportions for pregnancy outcomes were calculated using R software. Fourteen studies involving a total of 523 patients were analyzed. PRP administration was associated with a significant increase in EMT [MD=1.61 mm, 95% confidence interval (CI): 1.21-2.01, p<0.05]. The pooled clinical pregnancy rate following PRP treatment was 41.5% (95% CI: 29.6-53.9%). Corresponding rates for ongoing pregnancy, implantation, and miscarriage were 27.3% (95% CI: 19.7-35.0%), 22.9% (95% CI: 8.5-37.2%), and 5.3% (95% CI: 2.3-8.2%), respectively. Subgroup analyses suggested that heterogeneity was partly attributable to differences in study design and PRP administration route. Autologous PRP may be a safe and potentially effective adjunct to enhance endometrial receptivity and reproductive outcomes in women with thin endometrium. Although current evidence from single-arm studies provides a useful clinical reference, well-designed, large-scale randomized controlled trials are still needed to validate these findings.

Keywords: Platelet-rich plasma, thin endometrium, frozen-thawed embryo transfer, intrauterine infusion, meta-analysis

Öz

Dondurulmuş-çözülmüş embriyo transferi (FET) sikluslarına giren ince endometriumlu kadınlarda otolog trombositten zengin plazmanın (PRP) rahim içi infüzyonunun veya subendometrial enjeksiyonunun endometrium kalınlığı (EMT) ve gebelik sonuçları üzerindeki etkinliğini ve güvenliğini değerlendirmek. PubMed, Embase, Web of Science ve Cochrane Kütüphanesi'nde kapsamlı bir arama yapıldı. FET sikluslarında ince endometrium için PRP kullanan çalışmalar, sistematik derleme ve meta-analizler için tercih edilen raporlama öğeleri kılavuzlarına göre seçildi. Metodolojik kalite, Rastgele Olmayan Çalışmalar için Metodolojik İndeks aracı kullanılarak değerlendirildi. EMT için birleştirilmiş ortalama farkları (MD) ve gebelik sonuçları için birleştirilmiş oranları hesaplamak üzere R yazılımı kullanılarak tek kollu bir meta-analiz gerçekleştirildi. Beş yüz yirmi üç hastayı içeren on dört çalışma dahil edildi. Meta-analiz, PRP tedavisinin EMT'yi anlamlı derecede artırdığını göstermiştir [MD=1,61 mm, %95 güven arayığı (GA): 1,21-2,01, p<0,05]. PRP müdahalesinden sonra, birleştirilmiş klinik gebelik oranı %41,5 (%95 GA: %29,6-53,9) olmuştur. Devam eden gebelik oranı %27,3 (%95 GA: %19,7-35,0), implantasyon oranı %22,9 (%95 GA: %8,5-37,2) ve düşük oranı %5,3 (%95 CI: %2,3-8,2) olmuştur. Alt grup analizleri, çalışma tasarımının ve uygulama yolunun heterojenliğe katkıda bulunduğunu göstermiştir. Otolog PRP tedavisi, ince endometriyumlu hastalarda endometriyum reseptivitesini ve üreme sonuçlarını iyileştirmek için güvenli ve etkili bir strateji gibi görünmektedir. Mevcut tek kollu

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veriler umut vadeden bir klinik ölçüt öngörse de, bu bulguları doğrulamak için standartlaştırılmış büyük ölçekli randomize kontrollü çalışmalara ihtiyaç duyulmaktadır.

Anahtar Kelimeler: Trombositten zengin plazma, ince endometriyum, dondurulmuş-çözülmüş embriyo transferi, intrauterin infüzyon, meta-analiz

Introduction

Endometrial thickness (EMT) is a key determinant of embryo implantation and overall pregnancy outcome. Evidence indicates that insufficient EMT reduces implantation and pregnancy rates while simultaneously elevating the likelihood of early miscarriage, especially during frozen-thawed embryo transfer (FET) cycles[1,2]. Thin endometrium (TE) is characterized by inadequate endometrial thickness, often accompanied by reduced menstrual flow despite regular menstrual cycles, and is closely associated with a compromised reproductive prognosis[3]. In clinical practice, a cut-off value of 7 mm is generally accepted for the diagnosis of TE. This measurement is taken either on the day of oocyte retrieval [or human chorionic gonadotropin (hCG) trigger] during fresh in vitro fertilization (IVF) or upon commencement of progesterone in FET cycles[4]. Reports indicate that patients with an EMT ≤6 mm have pregnancy rates as low as 29.43%[5], suggesting a detrimental impact of TE on reproductive prognosis.

The treatment of TE remains a challenge in assisted reproduction. Although there is no universally accepted optimal treatment protocol, various strategies aim to promote endometrial proliferation[6,7]. Traditional treatment methods include the use of estrogen in artificial cycles, often in combination with low-dose aspirin, vitamin E, and vasodilators to improve blood flow and receptivity. However, these treatments often yield limited efficacy, and the endometrial recovery process in refractory patients is prolonged[8]. Consequently, there is an urgent need to develop safer and more efficient therapeutic strategies.

In recent years, autologous platelet-rich plasma (PRP), a bioactive preparation rich in growth factors, has demonstrated promising applications in the field of regenerative medicine. PRP is derived from peripheral blood and contains a high concentration of platelets[9,10]. Upon activation, these platelets secrete a vast array of bioactive molecules, including more than 800 proteins, cytokines, and hormones. These components are essential for driving angiogenesis, cell proliferation, and tissue repair[11,12]. Current clinical evidence indicates that administering autologous PRP, either through intrauterine infusion or sub-endometrial injection, can notably boost EMT and endometrial receptivity; this improvement, in turn, facilitates better outcomes regarding embryo implantation and pregnancy success[13,14]. For example, a study involving a cohort of 85 women with endometrial hypoplasia reported that intrauterine PRP infusion expanded the EMT by an average of 1.2 mm. Moreover, this intervention yielded a clinical pregnancy rate of 37%, which markedly surpassed the 20.2% rate observed in historical controls[15].

Although current research findings are encouraging, most existing studies have small sample sizes and heterogeneous study designs and PRP preparation protocols, leading to inconsistent conclusions. At present, key aspects of PRP application-such as preparation procedures (e.g., centrifugation parameters), routes of administration (intrauterine vs. sub-endometrial), and timing of intervention (e.g., days 10 to 13 of the hormone replacement cycle) have not been standardized. Furthermore, the safety profile of PRP therapy (e.g., risk of infection) and its long-term efficacy remain insufficiently explored. Moreover, the lack of consistent control groups across studies makes direct comparative analysis difficult. Therefore, performing a systematic review to derive a pooled efficacy estimate is essential for clarifying the actual therapeutic value of PRP.

To address this, we performed a comprehensive systematic review and a single-arm meta-analysis to assess the therapeutic efficacy of autologous PRP (administered via intrauterine infusion or sub-endometrial injection) for FET outcomes in patients with TE. By synthesizing data from existing single-arm and controlled trials, this study aims to establish clinical benchmarks for pregnancy rates and EMT improvement, providing evidence-based guidance for future research and clinical management.

Methods

Protocol and Guidance

This systematic review and meta-analysis was conducted according to the preferred reporting items for systematic reviews and meta-analyses guidelines and registered on PROSPERO (CRD420251043407) (Supplementary Table 1) [16].

Literature Search

A systematic search was performed across four electronic databases: PubMed, Embase, Web of Science, and the Cochrane Library. The literature search covered the period from database inception to April 2025. To ensure comprehensiveness, the reference lists of all included studies were also manually screened for additional relevant citations. The search terms included, but were not limited to, "PRP," "endometrial thickness," "embryo transfer," and "catheter". Detailed search strategies are provided in (Supplementary Table 2).

Eligibility Criteria

Inclusion and exclusion criteria were established based on the Participants, Intervention, Comparison, Outcome, and Study design framework.

Studies were included if they met the following criteria: (1): Participants (P): women diagnosed with a TE (<7 mm) undergoing FET cycles, irrespective of previous embryo transfer history, (2): Intervention (I): Intrauterine infusion or sub-endometrial injection of autologous PRP, with no restrictions on the mode or frequency of administration, (3): Comparison (C): Analysis of outcomes before and after intervention (self-controlled) or comparison with standard care or placebo (only PRP-arm data were extracted for this single-arm analysis), (4): Outcomes (O): The primary outcomes included changes in endometrial thickness, clinical pregnancy rate, chemical pregnancy rate, and ongoing pregnancy rate. Secondary outcomes included live birth rate, embryo implantation rate, miscarriage rate, and incidence of adverse events, (5): Study design (S): Randomized controlled trials (RCTs), non-RCTs, and observational studies (prospective or retrospective cohort studies).

Studies were excluded if they met the any of following criteria: (1): Conference abstracts, reviews, commentaries, case reports, or letters, (2): Animal studies, *in vitro* experiments, or other basic research, (3): Studies that did not involve the use of PRP, (4): Studies from which relevant data could not be extracted, (5): Studies for which the full text was unavailable.

Literature Management

Two researchers independently completed literature screening and data extraction. Any disagreements were resolved through discussion, and when consensus could not be reached, a third investigator was consulted. After removing duplicate entries using EndNote 21, we evaluated study eligibility by screening their titles and abstracts, which preceded detailed examination of the full texts.

Data Extraction and Quality Assessment

Relevant data were collected using a predefined Excel spreadsheet, covering study characteristics (including author, year, country, design, sample size, age, body mass index, infertility duration) and PRP-related details (including administration method and dosage). The methodological quality of the included studies was assessed using the Methodological Index for Non-Randomized Studies (MINORS) tool[17]. Quality assessment was conducted independently by two reviewers, with discrepancies resolved by discussion or adjudication by a third reviewer when necessary.

Definition of Outcome Measures

(1) Clinical pregnancy: The presence of a gestational sac with a fetal heartbeat identified by ultrasound 5 weeks after embryo transfer.

(2) Chemical pregnancy: Serum β-hCG ≥50 IU/L measured 14 days after embryo transfer.

(3) Ongoing pregnancy: Sustained intrauterine pregnancy beyond 12 gestational weeks.

(4) Miscarriage: Spontaneous pregnancy loss before 20 gestational weeks.

(5) Implantation rate: The ratio of gestational sacs to the number of embryos transferred.

(6) Live birth: Delivery of a viable neonate beyond 24 gestational weeks.

(7) hCG positivity: Early biochemical evidence of pregnancy (overlapping with chemical pregnancy in some reports).

Statistical Analysis

Statistical analyses were conducted in R (version 4.4.3) using the meta package. For binary outcomes (e.g., pregnancy rates), pooled proportions with 95% confidence intervals (CIs) were calculated. To stabilize the variance of proportions, the Freeman-Tukey double arcsine transformation was applied. For continuous variables (e.g., endometrial thickness), the mean difference (MD) representing the change from baseline (post-treatment minus pre-treatment) was calculated. Heterogeneity was assessed using I^2 and Cochran's Q test. I^2 >50% or $p<0.1$ indicated significant heterogeneity; in that case, a random-effects model was used; otherwise, a fixed-effects model was used. Subgroup analyses (by administration route, region, and study type) and sensitivity analyses (leave-one-out method) were conducted. For outcomes reported in ≥5 studies, publication bias was evaluated using funnel plots and Egger's test, with the trim-and-fill method applied if bias was present.

Results

Study Selection

A total of 95 records were identified through the systematic search (Figure 1). After the removal of 36 duplicate entries, 59 unique records remained for screening. Upon screening titles and abstracts, 36 studies were excluded for the following reasons: reviews or meta-analyses (n=2), conference abstracts

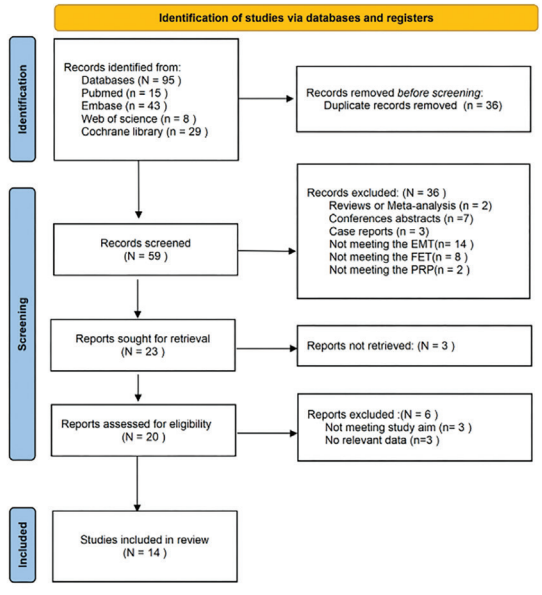

Figure 1. Flow chart of literature screening

(n=7), case reports (n=3), studies involving patients without a TE (n=14), studies not focusing on FET outcomes (n=8), and studies not involving PRP treatment (n=2). A further 23 studies were re-screened by full-text review; of these, 3 could not be accessed, 3 had research objectives unrelated to the topic, and 3 lacked relevant outcome data. Ultimately, 14 studies were included for analysis[4,14,18-29].

Study Characteristics and Quality Assessment

Fourteen studies that met the eligibility criteria were ultimately included in the analysis, encompassing 523 patients with TE whose mean age was 35.52±4.79 years. The study designs comprised 3 RCTs[19,25,26], 2 single-arm trials[18,24], 4 retrospective cohort studies[20,21,23,27], and 5 prospective cohort studies[4,14,22,28,29]. Regarding the method of PRP administration, 2 studies utilized subendometrial injection, 11 utilized intrauterine infusion, and 1 utilized both methods. The PRP injection doses ranged from 0.5 to 6 mL. The MINORS quality assessment revealed that, of the 14 studies, 12 were classified as high quality and 2 were of moderate quality. The fundamental characteristics and literature quality assessment results of the included studies are shown in Table 1.

Meta-analysis Results

Endometrial Thickness

Thirteen studies reported changes in EMT following PRP application during FET cycles in TE. The heterogeneity test indicated a high level of variability among studies (I^2=98.6%, p<0.0001); thus, a random-effects model was employed for analysis. The meta-analysis demonstrated that PRP significantly increases EMT (MD=1.61 mm, 95% CI: 1.21-2.01, p<0.05) (Figure 2A).

Because of substantial heterogeneity among the included studies, subgroup analyses were conducted to explore potential sources of heterogeneity based on study design, geographic region, and PRP administration methods (Supplementary Table 3). However, substantial heterogeneity persisted within these subgroups, suggesting that these factors may not fully explain the observed heterogeneity. Subgroup comparisons revealed that in RCTs, the increase in EMT following PRP treatment was significantly greater than in other study designs (MD=2.44 mm, 95% CI: 2.16-2.72). In Asian populations, the increase in EMT was 1.61 mm (95% CI, 1.21-2.07). Additionally, sub-endometrial injection resulted in a more pronounced increase in EMT compared to intrauterine infusion (MD=1.93 mm, 95% CI: 1.30-2.57).

Clinical Pregnancy Rate

Thirteen studies reported the clinical pregnancy rate following PRP treatment. Significant heterogeneity was observed (I^2=77.7%, p<0.0001), prompting the use of a random-effects model. The pooled clinical pregnancy rate after PRP treatment was 41.5% (95% CI: 29.6-53.9%) (Figure 2B).

Subgroup analyses were conducted to explore potential sources of heterogeneity (Supplementary Table 3). Despite stratification, high heterogeneity persisted. Subgroup analyses indicated that, in prospective cohort studies, the clinical pregnancy rate was 46.9% (95% CI: 6.7-89.4%). Furthermore, the clinical pregnancy rate following subendometrial injection was 47.2% (95% CI, 4.2-93.0%).

Chemical Pregnancy Rate

Five studies reported chemical pregnancy rates following PRP treatment. Due to high heterogeneity (I^2=90.3%, p<0.0001), a random-effects model was applied. The pooled chemical pregnancy rate was 23.5% (95% CI: 4.1-42.9%) (Figure 2C). Subgroup analyses (Supplementary Table 3) failed to fully account for the heterogeneity. However, comparisons revealed that in RCTs the chemical pregnancy rate was 40.0% (95% CI: 22.7-59.4%), whereas when PRP was administered via intrauterine infusion it was 29.8% (95% CI: 9.5-50.1%).

Ongoing Pregnancy Rate

Four studies reported the ongoing pregnancy rate following PRP treatment. No significant heterogeneity was observed among the studies (I^2=0.0%, p=0.40); thus, a fixed-effects model was employed. The pooled ongoing pregnancy rate was 27.3% (95% CI: 19.7-35.0%) (Figure 2D).

Miscarriage Rate

Six studies reported miscarriage rates following PRP treatment. No substantial heterogeneity was detected (I^2=10.3%, p=0.35); thus, a fixed-effects model was chosen to synthesize the data. The pooled miscarriage rate was 5.3% (95% CI: 2.3-8.2%) (Figure 2E).

Implantation Rate

Six studies reported the implantation rate following PRP treatment. High heterogeneity was observed (I^2=90.3%, p<0.0001), necessitating a random-effects model. The pooled implantation rate was 22.9% (95% CI: 8.5-37.2%) (Figure 2F).

Subgroup analyses (Supplementary Table 3) indicated that in RCTs, the implantation rate was 29.7% (95% CI: 10.1-49.3%). When PRP was administered via subendometrial injection, the implantation rate was notably higher, at 55.0% (95% CI: 31.5-76.9%).

Live Birth Rate

Seven studies reported live-birth rates following PRP treatment. Due to high heterogeneity (I^2=91.5%, p<0.0001), a random-effects model was employed. The pooled live birth rate was 23.6% (95% CI: 12.5-44.4%) (Figure 2G).

Subgroup analyses (Supplementary Table 3) showed that in retrospective cohort studies, the live birth rate was 42.4% (95% CI: 1.3-83.5%). Following subendometrial injection, the live birth rate was 37.9% (95% CI, 8.6-100.0%).

HCG Positivity Rate

Four studies reported hCG positivity rates following PRP treatment. Heterogeneity was significant (I^2=65.9%, p=0.032);

Table 1. Specific information about the included studies

Author	Year	Country	Study design	n	Age	BMI (kg/m2)	Duration of infertility (years)	PRP administration methods	PRP dosage	Outcome indicators	Minors
Cakiroglu et al.[7]	2025	Türkiye	NRCT	100	36.90±5.70	26.70±5.80	-	Injection	4-6 mL	①②⑦⑧	High
Eftekhar et al.[19]	2018	Iran	RCT	40	31.98±2.26	-	-	Infusion	0.5-1 mL	①②④⑤⑥	High
Coksuer et al.[20]	2019	Türkiye	Retrospective	34	29.41±4.54	26.35±4.41	7.66±2.87	Infusion	1 mL	②③⑤⑦	High
Dogra et al.[4]	2022	India	Prospective	20	32.35±3.89	25.60±4.14	7.85±4.61	Infusion	0.5-1 mL	①②⑥⑦	High
Fujii and Oguchi[21]	2024	Japan	Retrospective	70	38.30±0.50	22.50±0.40	3.10±0.20	Infusion	1 mL	①②③⑤⑦⑧	High
Gangaraju et al.[22]	2023	India	Prospective	9	33.67±6.46	-	-	Infusion	0.8 mL	①②	High
Shrivastava et al.[23]	2024	India	Retrospective	20	35.75±6.88	27.15±6.43	10.37±6.03	Injection	1 mL	①②③⑤⑥⑦	High
Kim et al.[14]	2019	Korea	Prospective	20	38.40±4.30	23.30±3.10	5.70±2.60	Infusion	0.7-1.0 mL	①②④⑥⑦⑧	High
Nagireddy et al.[24]	2019	India	NRCT	28	32.00±3.79	-	-	Infusion	-	①②④⑤⑥⑦	Moderate
Nazari et al.[25]	2019	Iran	RCT	30	33.93±2.76	24.30±2.24	-	Infusion	0.5 mL	①②③	High
Obidniak et al.[26]	2017	Russian	RCT	45	28-39	-	-	Infusion	2 mL	②⑥	Moderate
Wang et al.[27]	2024	China	Retrospective	47	36.90±1.13	21.61±0.61	2.09±0.68	Infusion	1 mL	①②④⑤⑧	High
Zadehmodarres et al.[28]	2017	Iran	Prospective	10	34.00±3.23	-	-	Infusion	0.5 mL	①③	High
Zaha et al.[29]	2023	Romania	Prospective	23	39.16±3.12	26.20±3.60	5.20±1.80	Infusion	2 mL	①	High
				27	37.26±2.32	24.50±5.80	3.40±1.40	Injection			

PRP: Platelet-rich plasma, BMI: Body mass index, RCT: Randomized controlled trial, NRCT: Non-randomized controlled trial, ①: Endometrial thickness, ②: Clinical pregnancy rate, ③: Chemical pregnancy rate, ④: Ongoing pregnancy rate, ⑤: Miscarriage rate, ⑥: Implantation rate, ⑦: Live birth rate, ⑧: hCG positivity rate:

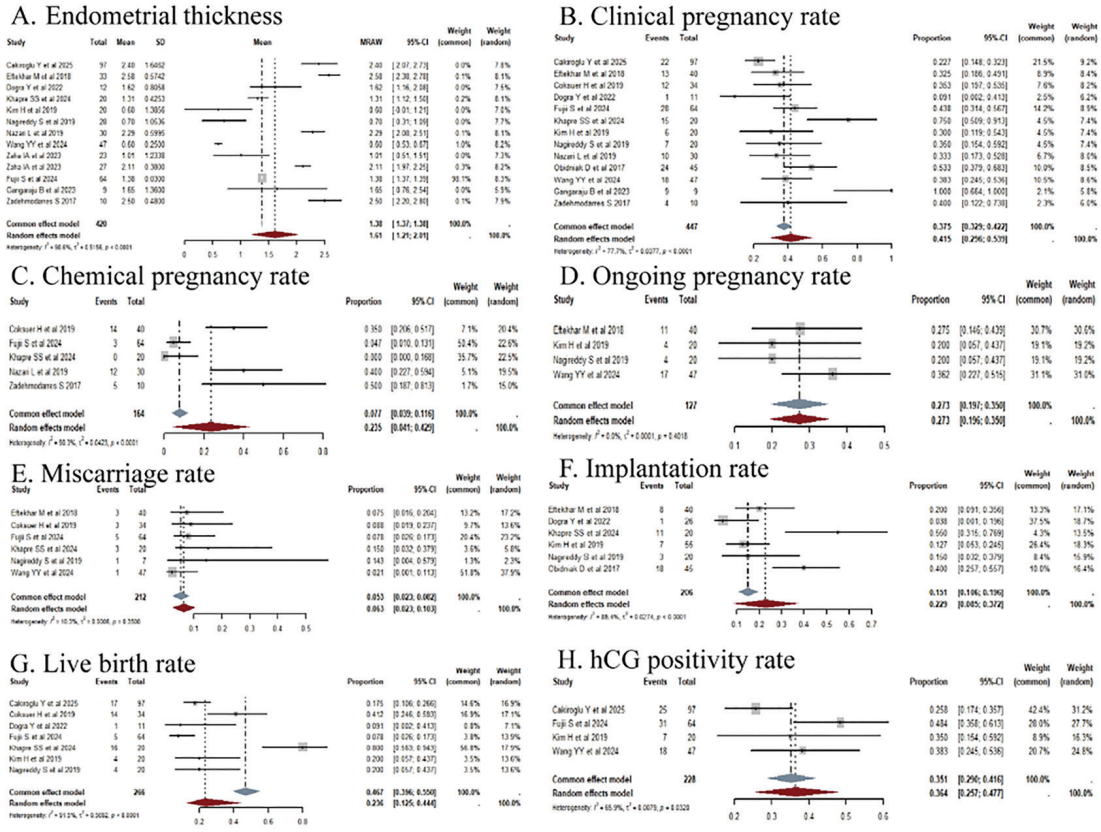

Figure 2. Forest plot of the effect of PRP on endometrial thickness and pregnancy outcomes

PRP: Platelet-rich plasma, hCG: Human chorionic gonadotropin

thus, a random-effects model was used. The pooled hCG positivity rate was 36.4% (95% CI: 25.7-47.7%) (Figure 2H). Subgroup analyses (Supplementary Table 3) indicated that both study design and PRP administration method contributed to heterogeneity. In retrospective cohort studies, the hCG positivity rate was 44.0% (95% CI: 34.4-53.9%). When PRP was administered via intrauterine infusion, the rate was 42.7% (95% CI: 34.2-51.4%).

Sensitivity Analysis and Publication Bias

A sensitivity analysis was performed using a leave-one-out approach for outcome measures that included more than five studies. Sensitivity analyses revealed that removal of any single study did not materially alter the pooled estimates for endometrial thickness, clinical pregnancy rate, chemical pregnancy rate, or miscarriage rate. These findings indicate a high degree of robustness and stability in the synthesized outcomes. As shown in Supplementary Figure 1.

For outcome measures with more than five included studies, publication bias was assessed using funnel plots and Egger's test. The results indicated no significant publication bias for EMT (p=0.58) and clinical pregnancy rate (p=0.16); both P-values exceeded 0.05. However, significant publication bias was detected for chemical pregnancy rate (p=0.02), miscarriage rate (p=0.02), implantation rate (p=0.02), and live birth rate (p=0.03); all p-values were <0.05. To further evaluate potential publication bias, we applied the trim-and-fill approach. After adjustment, the results suggested that the degree of publication bias was small and did not materially influence the reliability of the pooled outcomes. As shown in (Supplementary Figures 2-4).

Discussion

In this systematic review and single-arm meta-analysis, data from 14 relevant studies were pooled to assess the efficacy and safety of autologous PRP administered by intrauterine or subendometrial injection in women with TE. Overall, PRP administration was associated with significant gains in EMT and improvements across multiple reproductive endpoints, including pregnancy and implantation outcomes. These findings support the potential role of PRP in optimizing the endometrial environment and promoting receptivity.

This meta-analysis demonstrated that PRP treatment was associated with a meaningful increase in EMT, consistent with earlier reports. In a representative study by Kim et al.[14], 24 women with TE (EMT <7 mm) and a history of ≥2 failed IVF cycles were treated with two to three intrauterine PRP infusions, resulting in an average EMT gain of 0.6 mm

relative to the preceding cycle. Our subgroup analyses further suggested that the magnitude of benefit was greater in RCTs and that direct intra-endometrial administration produced more favorable outcomes than intrauterine infusion alone. Together, these observations imply that both the route and technique of PRP delivery may modulate treatment efficacy. From a biological perspective, PRP is enriched with multiple growth factors—including vascular endothelial growth factor, platelet-derived growth factor, transforming growth factor beta, and epidermal growth factor —which may collectively promote endometrial repair and receptivity in patients with TE[30]. These growth factors may enhance endometrial structure and function by promoting angiogenesis, epithelial cell proliferation, and stromal remodeling. Moreover, PRP may improve endometrial receptivity by modulating the local cytokine milieu and immunological microenvironment, thereby facilitating embryo implantation[31].

Regarding clinical pregnancy outcomes, the pooled clinical pregnancy rate following PRP intervention was 41.5%, which was comparable to or even exceeded that of conventional treatment strategies[19], and reached as high as 46.9% in some prospective studies. Furthermore, the ongoing pregnancy rate after PRP treatment was 27.3%, with a relatively low miscarriage rate of 5.3%, suggesting that PRP may not only enhance initial implantation but also contribute to pregnancy maintenance. This trend may be associated with PRP's ability to promote endometrial vascularization and stabilize the maternal-embryo interface. A notable improvement in implantation rate was also observed (22.9%), with even more pronounced effects reported in RCTs (exceeding 35%), supporting the viability of PRP as an adjunctive intervention. However, substantial variability was noted in chemical pregnancy rates, ranging from 4.1% to 42.9%, indicating high inter-study heterogeneity. Additionally, wide CIs were observed in certain subgroup analyses, likely due to the limited sample size of available studies. The observed heterogeneity may be attributable to differences in PRP dosage, timing of administration, and baseline endometrial conditions, thereby underscoring the need for standardized research designs and intervention protocols in future studies[32].

Study Limitations

Although the major outcomes demonstrated overall positive effects of PRP, several limitations remain: (1): The single-arm experimental design lacks a control group, which limits the ability to draw comparative inferences. However, subgroup data from RCTs consistently show that improvements with PRP are superior to those achieved with the standard hormone treatment regimen. (2): High heterogeneity was observed across key outcome variables. Even after performing subgroup analyses by study design, geographic region, and intervention mode, the sources of heterogeneity could not be fully accounted for. (3): The lack of standardization in PRP preparation and administration represents one of the most critical confounding factors affecting treatment efficacy. Considerable variability exists across studies regarding the source of PRP, centrifugation protocols, activation status, dosage, injection site, and frequency, all of which may directly influence the concentration of growth factors and subsequent biological effects[33]. (4): Beyond the PRP protocol itself, additional potential confounders include differences in the methods of EMT measurement, cycle regulation strategies (natural versus artificial cycles), and concomitant therapies such as estrogen supplementation or granulocyte colony-stimulating factor, which may further bias the meta-analytic results. (5): With regard to safety, no serious adverse events directly attributable to PRP have been reported to date, which is likely due to its autologous origin and low immunogenicity. However, invasive procedures, particularly subendometrial injection, may carry risks, including uterine perforation or infection, especially in the absence of standardized operating procedures; thus, they should be approached with caution. Moreover, incomplete reporting of adverse events in some studies limits the ability to perform a comprehensive assessment of long-term safety. (6): Currently, systematic research evaluating the long-term maternal and neonatal outcomes associated with PRP treatment, including potential birth defects and placental complications, is lacking. Accordingly, future research should focus on extended follow-up and the establishment of national or international prospective registries to systematically collect safety and outcome data. (7): Although correlations have been observed, causal mechanisms linking EMT to pregnancy success remain poorly defined, necessitating focused cellular, molecular, and translational studies.

Despite the aforementioned limitations, this study represents one of the few existing systematic reviews evaluating PRP treatment for TE, filling a critical gap in the current body of literature. As a low-cost, minimally invasive, and patient-friendly intervention, PRP has shown promise, particularly in TE patients who respond poorly to conventional therapies. Based on the findings of this analysis, future clinical applications may benefit from several strategic optimizations, including: (1): Optimizing the timing of intervention (e.g., intrauterine PRP infusion on days 10-12 of a hormone replacement cycle); (2): Developing standardized protocols for PRP preparation, including concentration grading, activation methods, and injection techniques; (3): Promoting multicenter, prospective RCTs with appropriately designed control groups (e.g., placebo or conventional treatment) to more accurately assess clinical efficacy; (4): Strengthening mechanistic studies to explore the roles of PRP in modulating endometrial immunity, activating stem cells, and enhancing the local microenvironment; (5): Establishing maternal-neonatal health outcome databases to systematically evaluate the potential impact of PRP on birth and long-term developmental outcomes.

Conclusion

Overall, autologous PRP administered via intrauterine infusion or sub-endometrial injection is associated with a significant increase in EMT in women with TE undergoing FET cycles. Available evidence also suggests potential benefits for pregnancy and implantation outcomes, with a possible reduction in miscarriage risk, supporting its role as a useful adjunct in clinical practice. Although heterogeneity and methodological differences remain across existing studies, PRP continues to show promise in assisted reproductive technology. Future research should prioritize well-designed, multicenter RCTs that integrate mechanistic insights with clinical outcomes and establish consensus protocols for treatment and safety evaluation to support evidence-based application in reproductive medicine.

Footnotes

Authorship Contributions

Concept: Z.T., Design: M.L., X.W., Data Collection or Processing: Z.T., X.W., Analysis or Interpretation: Ş.H., M.L., Z.T., X.W., Literature Search: M.L., Z.T., X.W., Writing: M.L., Z.T., X.W.

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