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Autologous Intrauterine Platelet-Rich Plasma Instillation In Repeated Implantation Failure In Assisted Reproductive Techniques

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ABSTRACT

Background: RIF (repeated implantation failure) represents a serious difficulty in reproductive medicine, and although numerous therapeutic approaches can be reported, there is no agreement on which is the most beneficial. Endometrium thickness was identified as a key determinant in the implantation of embryos. The purpose of this randomized controlled trial was to explore the advantages of platelet rich plasma (PRP) for thinning endometrial cases owing to its ability to promote endometrial growth and pregnancy outcome.

Aim of the work: PRP's involvement in RIF patients undergoing fresh & frozen embryo transfer cycles will be investigated, as well as the rates of implantation, chemical pregnancy, clinical pregnancy, and miscarriage.

Patients and methods: In this study, 104-women who had at least three failed embryo transfer cycle due to poor endometrial lining were candidates for frozen-thawed and fresh embryo transfer. Two groups of patients were formed: The study group (48 patients) got PRP intrauterine infusion. Control group who didn't practiced. When endometrium thickness is about 7 mm, embryo transfer was achieved. Endometrial thickness and clinical results were compared in the two groups.

Results: In the 13th day of the cycle, The Endometrial Thickness-(mm) were 7.1±0.01 for control and 8.1±0.054 for test group. The rate of implantation, chemical pregnancy, clinical pregnancy and misscarriage% were 34.8, 33.3, 22.9 and 10.4% for control group; and 58.5, 52.1, 45.8 and 6.3% for test group. The Endometrial Thickness (mm) expanded significantly to 7.23±0.11 and 8.3±0.60 mm in First PRP infusion and Repeated PRP infusion group, respectively. The PRP group had significantly greater implantation rates and clinical outcomes.

Conclusion: In women who have a history of thin endometrium, PRP may help to improve endometrial development and possibly pregnancy results.

Keywords: *Assisted Reproductive Technology (ART); Embryo transfer (ET); Platelet rich plasma (PRP); Repeated implantation failure (RIF).*

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INTRODUCTION

The lack of a gestational sac on ultrasonography 5 weeks or more following embryo transfer (ET) with high-quality embryos or following numerous transfers of 10 or more embryos is classified as repeated implantation failure (RIF)[1]. Endometrial receptivity, embryo quality, and immunological factors are among the many components implicated in the implantation process[2]. Several techniques to managing RIF have been successful, but there is little agreement on which is the most beneficial. Extra number embryo transfer, assisted hatching, co-culture system, preimplantation genetic screening (PGS), blastocyst transfer, endometrial scratching, sequential transfer, hysteroscopy, tubal disease salpingectomy, endometrial receptivity array (ERA), natural cycle, and immune therapy have all been used, but there is no proven evidence for these treatments[3,4].

The measurement of endometrial thickness has been used to predict implantation. With increasing endometrial thickness, the likelihood of conception rises. Various investigations have found that the minimal endometrial thickness for embryo transfer is greater than 7 mm. Kasius et al. (2014)[5] found that ET > 7 mm cases had a significantly higher chance of clinical pregnancy than ET ≤ 7 mm cases (48.1 compared with 23.3%). Conventionally many therapies have been tried in patients with nonoptimal endometrial lining, such as using of Estradiol valerate, intrauterine Granulocyte-colony stimulating factor instillation, use of Sildenafil, Human Chorionic Gonadotropin, low dose aspirin, but they lack consistency in delivering results[6,7,8].

Platelet-rich plasma (PRP) is a fraction of autologous blood plasma with platelet concentrations 4 to 5 times greater than usual[9]. It is prepared from fresh complete blood that has been stored in anticoagulant and processed to separate various components of blood to increase platelets[10]. Platelets contain a cocktail of chemical mediators including vascular endothelial growth factor, epidermal growth factor, transforming growth factor, and platelet-derived growth factor which activating platelets to become bioactive[9]. PRP has been utilized in surgery, wound healing, orthopaedics, and ophthalmology, for over a decade. It induces hard tissues regeneration such as tendons and bones, as well as soft tissues in injectable or gel form, like skin, fat, and mucosa[10]. PRP has been indicated to have a role in patients having thin refractory endometrium in limited studies, although its role in patients with implantation failures has received less attention[10,11]. PRP is utilized in reproductive medicine to boost implantation rates because it recruits growth factors that favor decidualization and implantation through a paracrine impact. Despite its widespread usage in a variety of medical sectors, PRP's use in reproductive medicine is limited[9]. PRP and its endometrial microvasculature biostimulation effects appear to be favorable to refractory endometrium patients, offering endometrial receptivity increase resulting in an increase in implantation rates, according to new findings. PRP intrauterine injection, according to many writers, can grow thin endometrium and increase pregnancy rates. In women who suffer from thin endometrium, PRP is a relatively recent procedure for increasing the thickness of the endometrium. PRP appears to be safe because it is produced from the sufferer's own blood[12].

In this case, there is a need to evaluate other modalities in this regard, as inadequate endometrial development or vascularity may result in repeated cycle cancellations or recurrent implantation failure, causing not only a psychological but also a financial burden on the patient. This pushes patients into surrogacy, which, given the medicolegal ramifications, may not be a realistic option right now. However, little is known in regard to PRP application's efficacy in the therapy of repeated implantation failure and improvement of pregnancy outcome; therefore, this study aimed to firstly, to assess the role of intrauterine infusion of autologous PRP on ET in ladies who underwent embryo transfer cycles (fresh and frozen) with suboptimal endometrial pattern as assessed by transvaginal ultrasound and secondarily, to study the implantation rate, and clinical outcomes including (rates of chemical pregnancy, clinical pregnancy and miscarriage).

PATIENTS AND METHODS

Criteria

After approval of the ethical committee, the participant patients were fully informed about protocol of the treatment and accordingly they signed consents to participate in the study. The following criteria were used to enroll patients in the research

Inclusion criteria

Age 18-35 years

Women who have had at least three unsuccessful embryo transfer cycles in the past (repeated implantation failure) due to poor endometrial lining.

Exclusion criteria

Age < 18 or > 35 years.

platelets < 150.000/mm^3.

Anticoagulant-treated patient.

NSAIDs were taken by the patient for ten days prior to the surgery.

Any major comorbidities or psychiatric illness which might threaten the patient 's consent.

A cervical or uterine infection that is active,

Women who have a recognized implantation failure reason, like poor embryo quality, Asherman syndrome, or congenital uterine abnormalities

Study procedure

From August 2019 to June 2021, one hundred and four women who had at least three failed embryo transfer cycles (repeated implantation failure) and had high-quality embryos who had been eligible for frozen-thawed and fresh embryo transfer have been eligible to participate in the study. Eight women were excluded for different reasons; 96 were included in the study. Two groups of patients were formed: The study group with 48 patients who underwent intrauterine infusion of PRP (divided into two subgroups frozen-thawed and fresh embryo transfer). While, control group contained 48 patients who did not practiced intrauterine infusion of PRP (divided into two subgroups frozen-thawed and fresh embryo transfer).

A 48 h prior to embryo transfer, a 0.5 ml intrauterine infusion of PRP containing 4-5 times more platelets than a peripheral blood sample is given. Serial transvaginal ultrasound examinations will be done using transvaginal probe of 5 to 9 MHz, on Logic V5 (Logic, GE Healthcare, India) starting from day 7/8, and repeated as required. The maximal distance across the endometrial canal from one basal endometrial interface to the opposite endometrial–myometrial interface after the patient has completely emptied her bladder is used to measure endometrial thickness in the uterus's median-longitudinal plane. In women who failed to achieve ET of 7 mm, intrauterine infusion of autologous PRP will be done for the same cycle after receiving written informed consent from the selected women A syringe with an anticoagulant is used to draw a sample of the blood of the patient (10 cm^3). PRP is obtained via sequential centrifugation (soft spin 200 g/15 min, then hard spin 600 g/6 min). PRP is infused intrauterine in a volume of 0.5-0.8 ml using an IUI cannula and ultrasound guidance while adhering to all aseptic measures. Repeat ultrasound will be done 72 h later by the same observer and the ET is noted. Second sitting of PRP infusion will be performed in a few patients who fail to show desired results. Embryo transfer is done in the patients who achieve a satisfactory endometrium (ET of 7 mm or more). 2

weeks later, serum beta hCG is measured and appropriate luteal phase support is provided. The rate of positive beta hCG and clinical pregnancy is calculated, as well as the rate of miscarriage. Statistical Package for the Social Sciences (SPSS) version 21 is used to analyze the data obtained. A P value of <0.05 is deemed statistically significant when using the paired t test.

Treatment assessment

A skilled ultra-sonographer measures endometrial thickness at the thickest section of the uterus' longitudinal axis. To validate thin endometrium, the thickness was measured three times and the mean of the three measurements had been taken. Endometrial thickness has been evaluated by transvaginal sonography as the primary endpoint, and clinical pregnancy following embryo transfer was the secondary endpoint. When a transvaginal ultrasound revealed an intrauterine gestational sac and an increase in serum β-HCG, clinical pregnancy was verified.

RESULTS

It was a randomized controlled trial in which one hundred and four ladies having a history of failed implantations who have been candidates for frozen-thawed and fresh embryo transfer were eligible to participate in the trial from August 2019 to June 2021. Eight ladies were disqualified for various causes; 96 were able to complete the study and their data were analyzed and included in the study. Two groups of patients were formed: The study group with 48 patients who received intrauterine infusion of PRP (divided into two subgroups frozen-thawed and fresh embryo transfer). While, control group contained 48 patients who did not practiced intrauterine infusion of PRP.

Table (1) presented baseline characteristics summary. The mean age, (BMI), history of previous uterine operations and history of previous Failed ET cycles of the study population (control vs. test) were 29.6±0.53, 24.6±0.55, 18(37.5%), 2-5 for control group and 28.4±0.67, 25.6±0.46, 21(43.8%), 2-5 for test group, respectively. The average age, (BMI), history of past uterine operations and history of previous Failed ET Cycles of the study population (control vs. test) were not significantly different.

Item	Control (no PRP)	Test (PRP ttt)	P value	Statistical method
n	48	48	-	-
Age (Year) (Mean±S.E)	29.6±0.53	28.4±0.67	**0.206**	**Two-tailed *t*-test**
BMI (Kg/m^2) (Mean±S.E)	24.6±0.55	25.6±0.46	**0.148**	**Two-tailed *t*-test**
History of previous uterine operations (n(%))	18(37.5%)	21(43.8%)	**0.473**	**Two-tailed *t*-test**
History of Previous Failed ET Cycles (Min.-Max.)	2-5	2-5	**0.808**	**Two-tailed *t*-test**

Mean±S.E; SE, Standard Error; BMI, Body Mass Index; PRP, Platelet Rich plasma; Min.-Max., Minimum-Maximum; * P value ≤ 0.05 is significant; ** P value ≤ 0.01 is significant.

Table 1: Patient's characteristics, general characteristics and IVF outcomes of patients of the study population.

Table (2) compares the study groups' embryo data as well as their clinical results. The rate of implantation (%), rate of chemical pregnancy (n(%)), rate of clinical pregnancy (n(%)) and rate of misscarriage (n(%)) were 34.8%, 16(33.3%), 11(22.9%) and 5(10.4%) for control group; and 58.5%, 25(52.1%), 22(45.8%) and 3(6.3%) for test group, respectively. The PRP group had a significantly higher rate of implantation and clinical pregnancy outcomes per cycle.

Item	Control group (n= 48)	PRP group (n= 48)	P value	Statistical method
Implantation Rate (%)	34.8%	58.5%	**0.003**	**Two-tailed *t*-test**
Chemical pregnancy Rate (n(%))	16(33.3%)	25(52.1%)	**0.038**	
Clinical pregnancy Rate (n(%))	11(22.9%)	22(45.8%)	**0.011**	
Misscarriage Rate (n(%))	5(10.4%)	3(6.3%)	**0.659**	

* P value ≤ 0.05 is significant; ** P value ≤ 0.01 is significant.

Table 2: The outcomes of embryo transfer cycles.

Table (3) provided and compared the embryo data as well as the research groups' clinical outcomes (Control and Test "PRP") as per kind of embryo transfer "fresh ET and frozen ET". The implantation rate (%), rate of chemical pregnancy (n(%)), rate of clinical pregnancy (n(%)) and rate of misscarriage (n(%)) for fresh ET were 31.8%, 7(29.2%), 5(20.8%), 2(8.3%) for control group; and 55.6%, 10(41.7%), 8(33.3%), 2(8.3%) for test group, respectively. While, for frozen ET were 37.8%, 9(37.5%), 6(25.8%), 3(12.5%) for control group; and 61.2%, 15(62.5%), 14(58.3%), 1(4.2%) for test group, respectively. The rate of implantation , as well as the rates of both

chemical and clinical pregnancy, were much greater in the frozen ET "PRP group," while the misscarriage rate was significantly reduced in comparison to the other group.

Item	Fresh ET				Frozen ET			
	Control (n=24)	PRP (n=24)	P value	Statistical method	Control (n=24)	PRP (n=24)	P value	Statistical method
Implantation Rate (%)	31.8%	55.6%	0.028	1.37	37.8%	61.2%	0.000	28.56
Chemical pregnancy rate (n(%))	7 (29.2%)	10 (41.7%)	0.083	1.81	9 (37.5%)	15 (62.5%)	0.011	2.769
Clinical pregnancy rate (n(%))	5 (20.8%)	8 (33.3%)	0.062	17.8	6 (25.8%)	14 (58.3%)	0.010	13.35
Misscarriage rate (n(%))	2 (8.3%)	2 (8.3%)	0.655	2.0	3 (12.5%)	1 (4.2%)	0.317	1.0

Note: Statistical method applied is Chi Square. * P value ≤ 0.05 is significant; ** P value ≤ 0.01 is significant.

Table 3: The outcomes of embryo transfer cycles according to type of embryo transfer.

Table (4) defined the cycle characteristics, including the number of transferred embryos plus embryo transfer stage and thickness of endometrium in the different study groups (Control and Test "PRP"). The No of transferred embryo (mean±s.e), embryo transfer stage including cleavage stage (n(%)) and blastocyst stage (n(%)) were 1.8±0.09, 20(41.7%) and 28(58.3%) for control group; and 2.1±0.11, 22(45.8%) and 26(54.2%) for test group, respectively. The transferred embryos number and embryo transfer stage indicated no significant differences among groups. Moreover, results presented in Table (4), showed that Average Endometrial Thickness (mm) (Mean±S.E) in the case of the first thickness of endometrium in the 13th day of the cycle (D1) the thickness of endometrium following intervention (D2) were 6.5±0.02 and 7.1±0.01 for control group; and 5.8±0.094 and 8.1±0.054 for test group, respectively. The first thickness of endometrium in the 13th day of the cycle (D1) and the thickness of endometrium following intervention (D2) showed no significant differences in control group but in test group was significantly difference.

Item		Control (n=48)	PRP (n=48)	P value	Statistical method
No of Transferred Embryo (Mean±S.E)		1.8±0.09	2.1±0.11	0.015	Two-tailed *t*-test 2.53
Embryo Transfer stage	• Cleavage stage (n(%))	20(41.7%)	22(45.8%)	0.758	Chi Square 0.095
	• Blastocyst stage (n(%))	28(58.3%)	26(54.2%)	0.785	Chi Square 0.074
	• P value	0.284	0.564	-	-
	• Statistical method	Chi Square 1.33	Chi Square 0.333	-	-
End. Thickness (mm)					
Average End. Thickness (Mean±S.E)	• Day 1	6.5±0.02	5.8±0.094	0.000	Two-tailed *t*-test 7.08
	• Day 2	7.1±0.01	8.1±0.054	0.000	Two-tailed *t*-test 17.8
	P value	0.062	0.005		
	Statistical method	Pearson test 17.8	Chi Square 177.1		

* P value ≤ 0.05 is significant; ** P value ≤ 0.01 is significant.

Table 4: Cycle characteristics in the transferred cycle.

Results presented in Table (5), showed the impact of Repeated PRP infusion on thickness of endometrium in comparison with First PRP infusion. The Endometrial Thickness (mm) (Mean±S.E) expanded significantly from 5.8±0.09 (Before) to 7.23±0.11 mm (After) with a difference of 1.46±0.03 mm in First PRP infusion group. While in Repeated PRP infusion group endometrial thickness was progressively expanded from 6.7±0.48 (Before) to 8.3±0.60 mm (After) with a difference of 1.62±0.12 mm. All the thickness of endometrium readings in the repeated PRP infusion were significantly different from those in the first PRP infusion (p-value: 0.000).

Item	First PRP infusion	Repeated PRP infusion	P value	Statistical method
End. Thickness (Mean±S.E)	5.8±0.09	6.7±0.48	0.000	Two-tailed *t*-test 6.3
• Before				
• After	7.23±0.11	8.3±0.60	0.000	Two-tailed *t*-test 6.71
• Difference	1.46±0.03	1.62±0.12	0.000	Two-tailed *t*-test 3.906

* P value ≤ 0.05 is significant; ** P value ≤ 0.01 is significant.

Table 5: Endometrial thickness in PRP group.

DISCUSSION

Human reproduction is a somewhat inefficient process, with cycle fecundity rates ranging from 20-25%, and this figure does not appear to increase greatly with assisted reproductive technology (ART), with reported cumulative pregnancy rates of 40-60%[13]. For successful implantation, a viable embryo, a receptive endometrium, optimal embryo – endometrial cross talk, and enough mother immune protection are all required. Changes in the techniques for ovarian stimulation and frozen embryo transfers have helped to improve ART outcomes. In addition, intrauterine instillation of granulocyte colony stimulating factor, endometrial scratching, and immunomodulators such as intralipids, IVIG, low-dose aspirin, and low-molecular-heparins have all been used to increase endometrial receptivity[14]. Despite these efforts, the rate of in vitro fertilization (IVF) pregnancy has not enhanced significantly in the last decade.

One of the most important variables for successful embryo implantation is endometrial thickness. In a typical human menstrual cycle, endometrium has become receptive during the implantation window, which occurs about days 19-23 in the natural cycle. Cytokines, adhesion molecules, prostaglandins, and growth factors are all produced at this time. Several research discovered that women who had RIF had lower levels of growth factor expression in their endometrium than women who are fertile[15]. As a result, endometrial preparation has become a critical stage in the embryo transfer process. Various therapy options, including vasoactive medications such as sildenafil citrate, low-dose aspirin, pentoxifyllinetocopherol, and extended estrogen delivery, have been investigated in recent years. Even with these treatments, a tiny percentage of women remained resistant, and ET cycles were frequently stopped by reason of the thin endometrium. The problem of efficient treatment for thin endometrium is yet unsolved. There would be an immediate need for new therapeutic techniques to increase endometrial thickness[12].

Platelets, which contain multiple sorts of granules elaborated in coagulation, inflammation, atherosclerosis, angiogenesis, and antimicrobial defense mechanisms due to their content of many growth factors, which include insulin-like growth factor, platelet-derived growth factor, vascular endothelial growth factor, and transforming growth factor, are the first cells to enter the injured site when tissue damage occurs. In numerous trials, PRP has been shown to minimize inflammation, postsurgical blood loss, infection, and the need for narcotics, and to accelerate osteogenesis, and soft tissue healing[16,17]. PRP's efficacy and safety have been reported in a variety of medical sectors, although there has been few clinical research to determine its significance. PRP is currently frequently used in therapeutic contexts, including in mucous tissues such as the eye and mouth, to enhance tissue regeneration, thanks to the actions of platelets. Furthermore, the combination of PRP with mesenchymal stem cells has been extensively researched in vitro[18]. Despite its widespread usage in a variety of medical sectors, PRP's use in reproductive medicine is limited. In patients with refractory endometrium, the endometrial microvasculature biostimulation effects of PRP appear to be favorable to increase endometrial receptivity and, as a result, the rate of implantation. PRP intrauterine injection, according to many writers, can grow thin endometrium and increase rates of pregnancy. PRP is a relatively recent procedure for endometrial thickness improvement in cases with thin endometrium[12].

The purpose of this research was to assess the effectiveness of PRP in the endometrial growth improvement, and possibly pregnancy results in ladies that failed to conceive following at least three failed embryo transfer cycle (repeated implantation failure). Our study revealed that the Endometrial Thickness (mm) in the 13th day of the cycle were 7.1±0.01 for control and 8.1±0.054 for test group. The implantation rate, chemical pregnancy, clinical pregnancy and misscarriage% were 34.8, 33.3, 22.9 and 10.4% for control group; and 58.5, 52.1, 45.8 and 6.3% for test group. The Endometrial Thickness (mm) expanded significantly to 7.23±0.11 and 8.3±0.60 mm in First PRP infusion and Repeated PRP infusion group, respectively. The PRP group had a considerably greater implantation and clinical pregnancy rates per cycle. According to our findings, PRP increased endometrial proliferation, rate of implantation, and rate of clinical pregnancy. A probable mechanism has been postulated by the presence of high quantities of many growth factors in PRP. For frozen ET cycle patients with thin endometrium, PRP intrauterine infusion might be a potential treatment option. PRP is made from autologous blood, thus there are no difficulties with transmission or immunogenic reactions. The therapy was declared safe in patients following hundreds of patients were managed with PRP following oral-maxillary surgery. Infection and other side effects are uncommon. After PRP infusion, no patient experienced any obvious side effects in this trial.

Chang *et al.* (2015)[10] used PRP in endometrial thickness improvement in patients suffer from thin endometrium, non-responsive to conventional treatment of estrogen, resulting in cancellation of cycle and low possibility of pregnancy through administration of an intrauterine PRP infusion in women who are infertile and have a thin endometrium. Five patients with a history of thin endometrium were enlisted in the study. PRP was injected into the uterus on the tenth day of a frozen ET cycle. PRP infusion was done 1-2 times in each cycle if endometrial thickness did not increase 72 hours afterwards. Once the endometrial thickness reached more than 7 mm, embryos were transplanted. During frozen ET cycles, four of five women having thin endometrium and a weak response to traditional treatment had a normal pregnancy, showing the effectiveness of intrauterine PRP injection for endometrial development in thin endometrium. The data will be used to support future large-scale randomized controlled trials in this discipline.

Nazari *et al.* (2016)[11] enlisted 20 people with a history of RIF in order to see how effective PRP is at

increasing pregnancy rates. They proved that PRP intrauterine injection had a positive effect on implantation and pregnancy. After PRP, 18 RIF women became conceived, with 16 pregnancies still going well and just one miscarriage and one molar pregnancy, indicating that PRP can help RIF patients have better pregnancy results. Tandulwadkar *et al.* (2017)[19] evaluated both the ET, vascularity clinical pregnancy rates and first trimester outcome after intrauterine PRP infusion. A relatively larger sample size of 68 patients was included in the study. They suggested that using autologous PRP to treat ladies with inadequate ET and vascularity for ET could be beneficial. The average pre-PRP endometrial thickness was 5 mm, whereas after PRP it grew to 7.22 mm. The amount of vascular signals seen on Power Doppler reaching zones 3 and 4 of the endometrium likewise showed a considerable increase in vascularity. The rate of clinical pregnancy was 45.31% and the rate of positive beta Human Chorionic Gonadotropin (hCG) was 60.93%. These findings matched those of Kim et al. (2019)[20], who found that PRP treatment increased the rates of implantation, pregnancy, and live delivery in women with refractory thin endometrium. According to their findings, PRP might greatly improve thin lining.

Chang *et al.* (2019)[21] investigated the effects of PRP in women who underwent frozen ET and had thin endometrium in a prospective cohort experiment. The endometrial thickness in the PRP group was substantially higher than in the control group (7.65 ± 0.22 vs. 6.52 ± 0.31 mm, respectively) and the PRP group has a lower cancelation rate (19.05 **vs.** 41.18%), having a higher rate of implantation and clinical pregnancy (27.94 vs. 11.67% respectively). Moreover, Chang *et al.* (2019)[21] analyzed the PRP solution, and the results proved the presence of higher levels of platelet-derived growth factor, and transforming growth factor in the PRP solution than the peripheral blood. El Hamedi and Salem (2019)[22] proved that platelet rich plasma is beneficial in stimulating endometrial growth, enhancing endometrial blood flow and thickness. This helped to increase the rate of pregnancy and rate of live birth in patients with repeated implantation failure due to poor endometrial growth and thin endometrial thickness.

CONCLUSION

The use of autologous platelet rich plasma intrauterine infusions to increase endometrial thickness in women undertaking fresh and frozen embryo transfer cycles with inadequate endometrial patterns has gotten a lot of attention. For women with thin endometrium, autologous PRP is a safe, easily accessible, and affordable therapeutic option. In conclusion, PRP effectively enhanced the thickness of the endometrium, rate of implantation, and rate of clinical pregnancy, according to our findings. The presence of high amounts of several bioactive components in PRP was suggested as a possible reason. For individuals with thin endometrium in a frozen ET cycle, PRP intrauterine infusion can be a successful alternate therapy. Increased endometrial thickness in patients following PRP infusion shows that intrauterine PRP infusion could be a unique treatment option for thin endometrium that hasn't responded well to conventional treatments. More research into the molecular basis of such a PRP therapy is required, as well as a well-designed large-scale prospective randomized clinical trial to uncover the exact mechanism and get more firm proof of PRP's positive effect on the endometrium in diverse pathologies.

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