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Original Research Article

Role of autologous platelet-rich plasma in improving endometrial receptivity in women undergoing ovulation induction

Pratibha Soni*, Ankita, Ruma Sarkar

Department of Obstetrics and Gynaecology, BRD Medical College, Gorakhpur, Uttar Pradesh, India

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***Correspondence:**
Dr. Pratibha Soni,
E-mail: pratibhasoni389@gmail.com

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ABSTRACT

Background: Thin endometrium and poor endometrial receptivity are significant barriers to conception in women undergoing ovulation induction. Platelet-rich plasma (PRP), an autologous blood product rich in growth factors, has shown promise in enhancing endometrial parameters and improving pregnancy outcomes. Objective: To evaluate the efficacy of intrauterine PRP infusion compared to standard estrogen therapy in improving endometrial receptivity and clinical pregnancy rates in women undergoing ovulation induction.
Methods: A prospective interventional study was conducted at BRD Medical College, Gorakhpur, including 150 women with poorly receptive endometrium. Participants were randomized into two groups: PRP group (n=75, receiving intrauterine PRP infusion) and control group (n=75, receiving oral estrogen therapy). Endometrial thickness, vascularity, echogenicity, and receptivity were assessed among both groups using transvaginal sonography and Uterine Scoring System for Reproduction (USSR).
Results: The PRP group showed a significant average increase in endometrial thickness+6.5 mm from baseline, compared to+4.6 mm in the control group ($p<0.001$). Improved endometrial vascularity (Grade 3 and Grade 4) was observed in 75% of the PRP group vs. 54.3% in controls. Positive β-hCG rates were 49.3% in the PRP group vs. 28% in the control group ($p<0.007$). Clinical pregnancy confirmed by fetal heartbeat occurred in 42.7% of PRP patients vs. 24% of controls ($p<0.01$). Ongoing pregnancy (>12 wks) were 34.7% in PRP group and 16% in control group ($p<0.008$).
Conclusion: PRP therapy is a promising, autologous, and cost-effective modality for improving endometrial receptivity in women undergoing ovulation induction.

Keywords: Platelet-rich plasma, Endometrial receptivity, Ovulation induction, Infertility, Endometrial thickness, Endometrial vascularity, Uterine scoring.

INTRODUCTION

Infertility is a growing public health concern globally, affecting millions of couples of reproductive ages. According to the World Health Organization (WHO), infertility is defined as the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse. Globally, the estimated prevalence of infertility is about 10–15% among couples.[1] In India, the burden of infertility is particularly significant due to a combination of sociocultural, lifestyle, and health-related factors. The National Family Health Survey-5 (NFHS-5, 2019–21) reported that approximately 18.7 per 1,000 women suffer from infertility based on the inability to conceive despite cohabiting for five or more years without contraception.[2] The aetiologies of female infertility are multifactorial, encompassing ovulatory disorders, tubal and peritoneal pathologies, uterine abnormalities, endometrial dysfunctions, and cervical issues. One of the key components in the establishment of pregnancy is a receptive endometrium.

It is estimated that nearly 60% of implantation failures can be attributed to defects in the endometrial environment.[3] To manage thin endometrium and enhance endometrial receptivity, several conventional therapies have been employed.[4,5] platelet-rich plasma (PRP) therapy has emerged as a novel and promising approach for the regeneration of thin or poorly responsive endometrium. PRP is an autologous blood product containing a high concentration of platelets suspended in plasma. It is rich in growth factors such as platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), transforming growth factor-beta (TGF-β), epidermal growth factor (EGF), insulin-like growth factor (IGF), and various cytokines. These biomolecules have been shown to promote angiogenesis, enhance cellular proliferation, modulate inflammation, and facilitate tissue repair.[6,7] In India, intrauterine PRP infusion significantly improved endometrial thickness and facilitated better embryo-endometrial synchrony in recurrent implantation failure patients,[3] PRP resulted in enhanced endometrial development and improved pregnancy outcomes in women with refractory thin endometrium.[6,8]

The study aims to evaluate the effectiveness of autologous PRP in improving endometrial receptivity among women undergoing ovulation induction. Specifically, also seeks to determine the role of autologous PRP in improving endometrial receptivity in women undergoing ovulation induction in terms of endometrial parameter improvement and also compare the use of autologous PRP with standard estrogen therapy in improving endometrial receptivity.

METHODS

Type of study:

Type of study was prospective interventional study.

Study place and time period

This study was conducted in Women aged 20–40 years with poorly receptive endometrium receiving an intrauterine infusion of PRP as case and age and BMI matched women with poorly receptive endometrium receiving standard estrogen therapy as control in the Departments of Obstetrics and Gynecology and Pathology at Nehru hospital, B.R.D. Medical College, Gorakhpur, over 12 months (January 2024–December 2024) after ethical approval.

Inclusion criteria

Inclusion criteria included women with thin endometrial**,** poor vascularity, repeated implantation failure and asherman's syndrome history with no adhesion at present.

Exclusion criteria

Exclusion criteria included women of reproduction age group having, congenital uterine anomaly, endometrial polyp or other growth, having uterine fibroid, women on anticoagulant or who had past uterine surgery.

A detailed history was taken for all participants, and a comprehensive physical examination was performed to record clinical parameters such as height, weight, BMI, and abdominal girth. Participants were divided into two groups: interventional group and control group. The cases consisted of 75 women who underwent intrauterine infusion of autologous PRP for poorly receptive endometrium, while the controls included 75 age- and BMI-matched women with thin endometrium undergoing ovulation induction with standard estrogen therapy. Randomization was done using computer generated tables.

Endometrial thickness, echogenicity, and vascularity were assessed using transvaginal sonography and the USSR scoring system.

Baseline endometrial thickness and other endometrial parameters, including echogenicity and vascularity were measured on day2 of menstrual cycle using transvaginal ultrasound. "The uterine scoring system for reproduction was used to assess the endometrium.''

Method to prepare PRP

Autologous PRP was prepared under aseptic conditions using a two-step centrifugation process. 7.5 ml of blood was drawn from patient in a syringe containing anticoagulant. PRP was obtained using sequential centrifugation soft spin at 1200 rpm for 10 minutes, which separated the specimen in 3 layers, which then is given hard spin of 2000 rpm for 10 min, to obtain supernatant which is used for instillation in intrauterine cavity using an intrauterine insemination IUI canula under ultrasound guidance following all aseptic precautions. On alternate days between cycle days 7–14, until endometrial thickness exceeded 7 mm with favorable vascularity.



Figure 1: (a) Preparation of platelet-rich plasma (PRP) and (b) prepared PRP intrauterine infusion within 30 min of its preparation.

Endometrial thickness, vascularity, echogenicity, and receptivity of women in both groups were assessed on days 2, 7, 9, 11, and 14 using transvaginal sonography and Uterine Scoring System for Reproduction (USSR). Pregnancy was confirmed through serum β-hCG and transvaginal ultrasound at 12 weeks.

RESULTS

In present study a total 150 cases, majority of the patients were in age group of 20-24 years in both PRP and control group. Total patient was categorized on the basis of Education, Area and socioeconomic status although the distribution varied across categories the difference was not statistically significant (Table 1).

In total 150 patients, majority of patients had primary infertility. The distribution of infertility duration was similar across both groups (Table 2).

On day 2, the endometrial thickness in the PRP group was 4.1±0.6 mm, which increased dramatically to 9.36±2.31 mm post-treatment. In contrast, the control group showed an increase from 4.0±0.5 mm to only 7.64±2.76 mm.

Table 1: Sociodemographic history outcome.

Parameters	Category	PRP Group (n=75)	Control Group (n=75)	P value
Age group (years)	20–24	39 (52.0%)	35 (46.7%)	0.56
	25–29	40 (40.2%)	22 (29.3%)	
	30–34	04 (5.3%)	15 (20.0%)	
	35–40	02 (2.7%)	03 (4.0%)	
Education	Illiterate	11 (14.7%)	09 (12.0%)	0.218
	Primary	28 (37.3%)	32 (42.7%)	
	Secondary	22 (29.3%)	28 (37.3%)	
	Graduate & above	14 (18.7%)	06 (8.0%)	
Area	Rural	53 (70.7%)	34 (45.3%)	0.002
	Urban	22 (29.3%)	41 (54.7%)	
Socioeconomic Status	Upper Middle	04 (5.3%)	01 (1.3%)	0.111
	Middle	43 (57.3%)	37 (49.3%)	
	Lower Middle	02 (2.7%)	08 (10.7%)	
	Lower	26 (34.7%)	29 (38.4%)	

Table 2: Obstetric history

Parameters	Category	PRP Group (n=75)	Control Group (n=75)	P value
Age group (years)	Primary	62 (82.7%)	67 (89.3%)	0.239
	Secondary	13 (17.3%)	08 (10.7%)	
Duration of Infertility	<3 years	18 (24.0%)	20 (26.7%)	0.971
	3–5 years	30 (40.0%)	28 (37.3%)	
	>5 years	27 (36.0%)	27 (36.0%)	

Table 3: Endometrial thickness

Parameter	PRP Group (Mean±SD /n=75)	Control Group (Mean±SD / n=75)	P value
D2 ET	4.1±0.6	4.0±0.5	0.283
D7 ET	6.2±0.71	5.83±0.62	<0.01
D10 ET	7.82±0.93	6.94±0.85	<0.001
D14 ET	9.36±2.81	7.64±2.76	<0.001
Pre-treatment ET	6.2±0.71	5.83±0.62	<0.001
Post-treatment ET	9.36±2.81	7.64±2.76	

The distribution of vascularity zones was as follows: in the PRP group, 4 (7.1%) participants were in Zone 1, 10 (17.9%) in Zone 2, 20 (35.7%) in Zone 3, and 22 (39.3%) in Zone 4. In the control group, 5 (14.3%) participants were in Zone 1, 11 (31.4%) in Zone 2, 12 (34.3%) in Zone 3, and 7 (20.0%) in Zone 4.

Multiple subcomponents of the USSR showed significantly superior outcomes on comparing the uterine scoring system of reproduction in both groups before and after treatment.

Table 4: Endometrial vascularity.

	PRP Group (Mean±SD /n=75)	Control Group (Mean±SD / n=75)	P value
Endometrial Vascularity - Zone 1	04 (7.1%)	05 (14.3%)	0.147
Endometrial Vascularity - Zone 2	10 (17.9%)	11 (31.4%)	
Endometrial Vascularity - Zone 3	20 (35.7%)	12 (34.3%)	
Endometrial Vascularity - Zone 4	22 (39.3%)	07 (20.0%)	

Table 5: USSR grading in PRP and control group (pre & post PRP treatment)

S. no.	Parameter Description	Score	Category	PRP Group N (%) – Pre	Control Group N (%) – Pre	PRP Group N (%) – Post	Control Group N (%) – Post	P value (Pre)	P value (Post)
1	Endometrial thickness	0	<7 mm	28 (37.3%)	30 (40.0%)	6 (8.0%)	14 (18.7%)	0.72	0.005
		2	7–9 mm	34 (45.3%)	35 (46.6%)	12 (16.0%)	21 (28.0%)		
		3	10–14 mm	13 (17.3%)	10 (13.3%)	57 (76.0%)	40 (53.3%)		
2	Endometrial layering	0	No layering	11 (14.7%)	13 (17.3%)	4 (5.3%)	10 (13.3%)	0.83	0.03
		1	Hazy 5 lines	40 (53.3%)	39 (52.0%)	18 (24.0%)	25 (33.3%)		
		3	Distinct 5 lines	24 (32.0%)	23 (30.7%)	53 (70.7%)	40 (53.3%)		
3	Endometrial motion	0	<3 contractions in 2 min	51 (68.0%)	52 (69.3%)	23 (30.7%)	36 (48.0%)	0.78	0.03
		3	>3 contractions in 2 min	24 (32.0%)	23 (30.7%)	52 (69.3%)	39 (52.0%)		
4	Myometrial echogenicity	1	Coarse, inhomogeneous	48 (64.0%)	46 (61.3%)	22 (29.4%)	38 (50.7%)	0.81	0.04
		3	Relatively homogeneous	27 (36.0%)	29 (38.7%)	53 (70.6%)	37 (49.3%)		
5	Uterine artery doppler (pi)	0	>3	12 (16.0%)	13 (17.3%)	3 (4.0%)	10 (13.3%)	0.89	0.007
		0	2.5–2.99	19 (25.3%)	20 (26.6%)	9 (5.3%)	13 (17.3%)		
		1	2.2–2.49	18 (24.0%)	18 (24.0%)	10 (13.3%)	15 (20.0%)		
		2	<2.19	26 (34.7%)	24 (32.0%)	53 (70.7%)	37 (49.3%)		
6	Endometrial blood flow (zone iii)	0	Absent	14 (18.6%)	13 (17.3%)	2 (2.6%)	5 (6.6%)	0.74	0.08
		2	Sparse blood flow	34 (45.3%)	33 (44.0%)	18 (24.0%)	28 (37.3%)		
		5	Multifocal blood flow	27 (36.0%)	29 (38.7%)	55 (73.3%)	42 (56.0%)		
7	Myometrial blood flow (angiographic)	0	Absent	41 (54.7%)	44 (58.7%)	4 (5.4%)	10 (13.3%)	0.67	0.008
		1	Present	34 (45.3%)	31 (41.3%)	71 (94.6%)	65 (86.6%)		

Table 6: Biochemical pregnancy, clinical pregnancy and ongoing pregnancy.

Parameters	Category	PRP Group (n=75)	Control Group (n=75)	P value
1. β-HCG	Negative	38 (50.7%)	54 (72.0%)	0.007
	Positive	37 (49.3%)	21 (28.0%)	
2. Clinical Pregnancy	Absent	43 (57.3%)	57 (76.0%)	0.01
	Present	32 (42.7%)	18 (24.0%)	
3. Ongoing Pregnancy (>12 weeks)	Absent	49 (65.3%)	63 (84.0%)	0.008

The most clinically "relevant outcomes of this study were the biochemical, clinical, and ongoing pregnancy rates. PRP-treated participants demonstrated significantly higher β-hCG positivity (49.3%) compared to the control group (28.0%) (p=0.007). Clinical pregnancy, defined by the presence of an intrauterine gestational sac on transvaginal ultrasound, was also significantly more frequent in the PRP group (42.7% vs. 24.0%, p=0.01). Importantly, the

ongoing pregnancy rate—defined as viable gestation beyond 12 weeks—was 34.7% in the PRP group versus 16.0% in the control group (p=0.008).

DISCUSSION

Group A patients received autologous platelet rich plasma while Group B received standard estrogen therapy. The baseline characteristics of both groups were comparable in terms of age, body mass index (BMI), socioeconomic status, education level, and clinical infertility history. The mean age of women in the PRP group was 24.79±3.26 years, while that in the control group was 25.61±4.35 years (p=0.191). This distribution mirrors that of earlier studies, including those by Singh et al (2024) [10] and Dogra et al. (2024) ,[8] where PRP was most commonly administered in younger women of reproductive age between 20 and 30 years.[1,9]

The area of residence showed a statistically significant difference, with a higher proportion of rural participants in the PRP group (70.7%) compared to 45.3% in the control group (p=0.002). Despite this disparity, outcomes favored the PRP group, reinforcing its efficacy and feasibility even in less resource-rich settings. This supported the conclusions of Dutta et al and Karadbhajne et al, who highlighted the affordability and scalability of PRP in public health contexts.

The PRP group had 82.7% of participants with primary infertility and 17.3% with secondary infertility, while the control group had 89.3% primary and 10.7% secondary infertility. The difference between groups was not statistically significant (p=0.239), ensuring comparability in baseline infertility types. In a recent study by Chang et al. (2023), although the focus was primarily on the mechanisms of PRP in enhancing endometrial receptivity, the population also predominantly included women with primary infertility. Their study supported PRP's role in creating a more favorable intrauterine environment, irrespective of infertility type, by modulating immune responses and enhancing vascularity.[13]

The distribution of infertility duration was similar across both groups:

<3 years: 24.0% PRP vs. 26.7% (Control),3–5 years: 40.0% PRP vs. 37.3% (Control),> 5 years: 36.0% (both groups). In comparison, Chang et al. (2023) primarily emphasized the biological role of PRP in enhancing endometrial receptivity and did not stratify outcomes based on infertility duration.[13]

One of the most striking findings of this study was the significant enhancement of endometrial thickness following PRP infusion. On Day 2, the endometrial thickness in the PRP group was 4.1±0.6 mm, which increased dramatically to 9.36±2.31 mm post-treatment. In contrast, the control group showed an increase from 4.0±0.5 mm to only 7.64±2.76 mm, and the inter-group difference was statistically significant (p<0.001). This 3-fold increase in endometrial thickness in the PRP group echoes the findings of Noushin et al (2021), and Maleki-Hajiagha et al (2020) who reported substantial improvements in women with refractory thin endometrium following PRP administration.[14,15]

The temporal effect of PRP on endometrial thickness was evident from serial ultrasonographic measurements. On Day 7 of the cycle, the endometrial thickness was significantly higher in the PRP group (6.20±0.71 mm) compared to the control group (5.83±0.62 mm, p=0.01). This trend continued on Day 10 (7.83±0.93 mm vs. 6.94±0.85 mm; p<0.001) and Day 14 (9.36±2.31 mm vs. 7.64±2.76 mm; p<0.001), illustrating sustained endometrial growth. These improvements align with the early proliferative changes described in studies by Wang et al (2024) and Rahmatullah et al (2021), who linked PRP's effect to rapid recruitment of epithelial and stromal progenitor cells stimulated by growth factors.[16,17]

In this study, endometrial vascularity, assessed via power Doppler, showed significant improvement in the PRP group compared to controls. This difference highlighted the potential of PRP to promote angiogenesis, a conclusion supported by the upregulation of vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and other pro-angiogenic molecules released by activated platelets. A closer look at vascular penetration zones revealed a trend toward deeper stromal perfusion (Zone 4) in the PRP group (39.3%) compared to controls (20.0%), though this did not reach statistical significance. Nonetheless, the presence of deep vascularity is a positive prognostic indicator. Zeffiro et al emphasized that adequate Zone 3/4 blood flow correlates with improved embryo implantation and clinical pregnancy.[18]

The uterine scoring system for reproduction (USSR), a composite ultrasound index for assessing endometrial receptivity, further validated the benefits of PRP. Before treatment, there were no statistically significant differences between the PRP and control groups in any of the USSR grading parameters. This suggests that both groups were well-matched in terms of baseline uterine receptivity scores. For example: Endometrial thickness of ≥10 mm was observed in 17.3% of the PRP group vs. 13.3% in the control group (p=0.72). The characteristic trilaminar or "five-line" pattern was observed in 32.0% of PRP patients versus only 30.7% in the control group (p=0.83) Similarly, multifocal blood flow was present in 36.0% of PRP vs. 38.7% of controls (p=0.74). All other features, including myometrial echogenicity, uterine artery Doppler (PI), and myometrial blood flow with zone III, showed comparable distribution. The pre-PRP treatment USSR profile in this study confirms a high prevalence of suboptimal uterine receptivity indicators. No statistically significant differences were observed at baseline between PRP and control groups across all USSR parameters (p>0.05). Multiple subcomponents of the USSR showed significantly superior outcomes on comparing the uterine

scoring system of reproduction in both groups after treatment. i.e., 76% of PRP participants had an endometrial thickness ≥10 mm compared to 53.3% of controls (p=0.005). The characteristic trilaminar or "five-line" pattern was observed in 70.7% of PRP patients versus only 53.3% in the control group (p=0.03), indicating better stromal organization. Moreover, uterine artery resistance indices, represented by Pulsatility Index (PI), were more favorable in the PRP group; 70.7% had PI<2.19, compared to 49.3% in controls (p=0.007). Post-PRP treatment USSR profile showed statistically significant improvement in several uterine parameters in the PRP group compared to the control group. All of these ultrasound markers have been independently associated with improved implantation potential, and their collective presence strongly supports the enhanced receptivity achieved by PRP therapy and all of which are predictive of better implantation rates. These findings corroborate the results of Efendieva et al and Tej et al, who observed similar improvements in uterine scoring and perfusion following intrauterine PRP administration.

The most clinically relevant outcomes of this study were the biochemical, clinical, and ongoing pregnancy rates. These findings are echoed by a multitude of studies. Maleki-Hajiagha et al, in their 2020 meta-analysis involving 9 RCTs, reported that intrauterine PRP significantly improves implantation and clinical pregnancy rates compared to controls.[15] Further support comes from prospective trials by Noushin et al and Wang et al, where PRP significantly enhanced both biochemical and clinical pregnancy outcomes in women with refractory thin endometrium.[16,21]

CONCLUSION

This study affirms the significant potential of autologous PRP as an effective adjunctive therapy to improve endometrial receptivity in infertile women undergoing ovulation induction. Among 150 participants, those receiving PRP infusions demonstrated superior outcomes compared to those on standard therapy, including significantly increased endometrial thickness, enhanced vascularity, and improved uterine receptivity markers such as trilaminar pattern and optimal Doppler indices.

Clinically, the PRP group had higher biochemical, clinical, and ongoing pregnancy rates, indicating not only enhanced implantation but also support for early gestation. The therapy showed a dose-dependent benefit, with multiple infusions yielding better outcomes in resistant cases.

Importantly, PRP was well tolerated, with no serious adverse events reported. As an autologous and biologically safe product, it offers a low-risk, cost-effective, and minimally invasive alternative, particularly useful for women with thin endometrium or repeated implantation failure. It also has the potential to reduce treatment cycles, enhance patient satisfaction, and ease the emotional and financial burden of infertility.

The study highlights PRP's dual role of anatomical improvement and biological support for embryo development and encourages its broader use in infertility management. However, future research is recommended to standardize PRP protocols, investigate molecular mechanisms, assess long-term outcomes (e.g., live birth and neonatal health), and conduct comparative trials against other intrauterine therapies to optimize clinical application.

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