INTRAUTERINE PLATELET-RICH PLASMA INFUSION FOR RECURRENT IMPLANTATION FAILURE: A PILOT RANDOMIZED CONTROLLED SINGLE-BLINDED CLINICAL TRIAL

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Background
Recurrent implantation failure (RIF) is a challenging clinical dilemma with no proven standard treatment. Platelet-rich plasma (PRP) has been used in several clinical scenarios with proposed benefits in restoring tissue function. Several studies from outside the US have reported improved pregnancy rates in RIF with intrauterine PRP infusion [1].
Objective
To study the therapeutic effect of intrauterine PRP infusion in patients with RIF after frozen embryo transfer (FET) cycles in a randomized control single-blinded clinical trial.
Materials and Methods
Patients with RIF were randomized to treatment or sham-control arms along with standard therapies. Inclusion criteria were ≥2 failed embryo transfers with autologous or donor egg embryos and endometrial thickness > 7mm. PRP was isolated from peripheral blood using the Magellan® concentration system, and 1 mL of PRP was infused into the uterine cavity. Control patients received an infusion of saline. Two intrauterine infusions were performed: cycle day 9-12 (or 10-14 days of estradiol in a programmed cycle) and 2-3 days prior to transfer. Testing for endometrial receptivity and chronic endometritis were performed at physician discretion in both groups. Patients randomized to the control group were offered PRP in a subsequent cycle if they did not conceive with initial FET. The primary outcome was live birth rate (LBR). The secondary outcomes were overall pregnancy rate (PR), clinical pregnancy rate (CPR), miscarriage rate (MR), and endometrial thickness (EMT) per completed cycle. Statistical differences were evaluated using Wilcoxon rank sum test, Fisher's exact test and Pearson's Chi-squared test.
Results
Thirty-nine patients were randomized, 6 patients did not complete an FET due to study withdrawal or cycle cancellation, and 33 patients underwent their assigned treatment for their first FET (Control n = 20, PRP n=13). Notable demographic data and pregnancy outcomes for patients in the primary analysis are shown in **Table 1**. Otherwise, there were no differences in current FET protocol use, hemoglobin/platelet count, number of embryos transferred, embryo grade or ploidy status. A similar number of patients underwent testing for endometrial receptivity, chronic endometritis and ReceptivaDx. In the primary analysis, LBR was 46% vs 25% (p=0.3) in PRP vs control groups, respectively. There was no difference in EMT between treatment groups. Eight patients who did not conceive following randomization to the control group crossed over to pursue an additional FET with PRP with one additional live birth (for a total of 21 patients receiving PRP in this study). PRP was well tolerated with no adverse events.
Conclusion
While no statistically significant improvement in clinical outcomes was observed, there was a possible trend for improved LBR and lower MR. PRP infusion was well tolerated. This pilot study suggests a positive impact of PRP in RIF patients, but a larger multi-site study is warranted to confirm generalizability in the US RIF population.
Support:
Stanford SPARK Translational Research Program Grant (LA).

References:

1. Anitua E *et al.* 2023. Efficacy of platelet-rich plasma in women with a history of embryo transfer failure: a systematic review and meta-analysis with trial sequential analysis. Bioengineering 10(3): 303.

Table 1. Demographic parameters and outcomes of patients included in this study.

	Control (N=20)	PRP (N=13)	p
Age	37.0 (35.0, 40.3)	37.0 (34.0, 39.0)	0.4
BMI	25.7 (23.1, 27.9)	23.9 (22.1, 28.3)	0.6
Number failed transfers			0.7
2	11 (55%)	7 (54%)	
3	9 (45%)	5 (38%)	
4	0 (0%)	1 (7.7%)	
Embryo Day			**0.013**
5	17 (85%)	6 (46%)	
6	2 (10%)	7 (54%)	
7	1 (5.0%)	0 (0%)	
PGT-A	18 (90%)	10 (77%)	0.4
Endometrial thickness (trigger/P4 start)	8.20 (8.00, 9.45)	8.40 (8.00, 9.00)	>0.9
Overall Pregnancy	10/20 (50%)	9/13 (69%)	0.3
Clinical Pregnancy	6/20 (30%)	8/13 (62%)	0.073
Live Birth	5/20 (25%)	6/13 (46%)	0.3
Ectopic Pregnancy	0/20 (0%)	1/13 (7.7%)	0.4
Multi-fetal Gestation	1/20 (5%)	0/13 (0%)	>0.9
Miscarriage Rate	5/10 (50%)	2/9 (22%)	0.3
Clinical Miscarriage Rate	1/10 (10%)	2/9 (22%)	0.6
Biochemical Miscarriage Rate	4/10 (40%)	0/9 (0%)	0.087