Comparison of Outcomes of Frozen Embryo Transfer using Endometrial Preparation with Lupron versus Estrogen Only

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Introduction

Frozen Embryo Transfer (FET) has become increasingly more common in the standard of care for in vitro fertilization (IVF). There are two common protocols for preparation of a medicated embryo transfer: estrogen only (EO) and Lupron downregulation preceding estrogen supplementation (LDR). Lupron is a gonadotropin-releasing hormone (GnRH) agonist which targets the pituitary gland to stimulate the production of FSH and LH, hormones which regulate the growth and ovulation of oocytes. When used constitutively, a GnRH agonist will result in a downregulation of this production, effectively mitigating any ovarian interference during a treatment cycle for embryo transfer, but the use of Lupron increases both time and cost of a cycle compared to estrogen only. Currently, studies are conflicting as to which protocol is superior, EO vs LDR. We performed a retrospective analysis of pregnancy outcomes in patients undergoing FETs within our own institution.

Methods

All patients undergoing FET from a single private practice facility from January 1st, 2018, to December 31st, 2019, were included in this retrospective cohort study. There was a total of 434 embryo transfers from 339 patients. Information regarding demographics, patient history, prior fertility treatment, thaw and transfer data, laboratory values, FET protocol, and pregnancy outcomes were all extracted from the Fertility Answers® records. Of the 434 embryo transfers, 235 FETs used LDR, and the other 174 FETs were EO serving as the control group. Statistical analysis compared live birth rates and spontaneous abortions between the two groups.

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Baseline Characteristics

Table 1. Baseline Characteristics

Characteristic	EO (N=174)		LDR (N=235)	
Race				
Black	11	6.3%	31	13.2%
White	150	86.2%	194	82.6%
Asian	5	2.9%	6	2.6%
American Indian	2	1.1%	0	0.0%
NR	6	3.4%	4	1.7%
Ethnicity				
Hispanic	3	1.7%	4	1.7%
Non-Hispanic	152	87.4%	216	91.9%
NR	19	10.9%	15	6.4%
SART Diagnosis				
Didelphys	2	1.1%	0	0.0%
DOR	22	12.6%	37	15.7%
Endometriosis	11	6.3%	16	6.8%
Male factor	62	35.6%	53	22.6%
PCOS	29	16.7%	24	10.2%
Tubal factor	22	12.6%	56	23.8%
Unexplained	22	12.6%	46	19.6%
Unicornuate	1	0.6%	0	0.0%
NR	3	1.7%	3	1.3%
Patient History				
Tobacco use	7	4.0%	9	3.8%
Metformin use	42	24.1%	27	11.5%
Prior FETs	81	46.6%	135	57.4%

Table 1. Baseline characteristics are demonstrated for both the EO and LDR groups of FETs. The raw data indicate the number of transfers in which each characteristic applied.

Results

Table 2. Live Birth Rates

	Live Births			
	Y	N	%	p-value
Estrogen only	71	103	40.8	0.27
Lupron + Estrogen	109	126	46.4	

Table 2. Live birth rates are compared between the EO and LDR groups. The p-value is 0.27.

Table 3. Spontaneous Abortion Rates

	Spontaneous Abortions			
	Y	N	%	p-value
Estrogen only	32	142	18.4	0.0625
Lupron + Estrogen	27	208	11.5	

Table 3. Spontaneous abortion rates are compared between the EO and LDR groups. The p-value is 0.0625.

Results (cont.)

Table 4. Preimplantation Genetic Screening prior to FET

	PGS			
	Y	N	%	p-value
Estrogen only	121	53	69.5	0.0054
Lupron + Estrogen	131	104	55.7	

Table 4. The number of euploid embryos confirmed by Preimplantation Genetic Screening (PGS) in both the EO and LDR groups are compared. The p-value is 0.0054.

The baseline characteristics between the EO and LDR groups show no statistical differences (Table 1). When comparing live birth rates between both groups, the LDR group demonstrated a slightly higher live birth rate (46.4%) than the EO group (40.8%, Table 2); however, this did not reach statistical significance, p-value = 0.27.

When comparing spontaneous abortions between the two groups, the LDR group demonstrated a trend towards lower rate of spontaneous abortions when compared to the EO group (11.5% vs 18.4%, p=0.0625; Table 3). This was despite noting that the number of FETs that used Preimplantation Genetic Screening (PGS) in the EO group was higher (69.5%) compared to the LDR group (69.5% vs 55.7%, p-value = 0.005).

Conclusion

In our study, there was no clear benefit of using LDR over EO for endometrial preparation in frozen embryo transfer cycles. Interestingly, there was a trend towards higher miscarriage rate in the EO group, despite having a higher number of embryo transfers with PGS. With more euploid embryo transfers, one might expect to see better pregnancy outcomes in the EO group, but this was not the case, rather the LDR was slightly higher (46% vs 41%, Table 2). This may be due to a lack of power in our sample size, a limitation of any retrospective study. Indeed, it may be that LDR benefits specific subsets of the patient population. Factors such as age or SART diagnosis could be analyzed in isolation to determine if a superior protocol exists in these individual groups. Future studies with more patients will allow for a more robust analysis and answer to this important clinical question.