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Title:

AN OBSTETRICAL PERSPECTIVE: THE BENEFITS OF A FROZEN EMBRYO TRANSFER CYCLE

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Objective:
The paradigm of reproductive care has shifted with the developments of embryo cryopreservation and preimplantation genetic testing (PGT). As compared to a fresh transfer approach, a frozen embryo transfer (FET) presents a physiologic hormonal milieu similar to a natural cycle and has shown to favor implantation due to improved embryo-endometrial synchrony. Still, the benefits of a FET cycle do not offset obstetrical concern, such as abnormal placental adherence and large for gestational age (LGA) infants. The study sought to compare perinatal outcomes of fresh versus frozen SETs.

Design:
Retrospective cohort study

Materials and Methods:
The single institution study included patients who achieved a live singleton birth after a fresh or frozen blastocyst SET from 2004 to 2016. Donor oocyte IVF cycles were excluded. SET cycle characteristics, demographic information, prenatal and obstetrical data were compared according to fresh ET vs. FET. Student's t-test, chi square, fisher's exact test, linear and binary logistic regression analysis were used.

Results:
Three hundred twenty-three patients underwent SET cycle (Fresh (n=138) or Frozen (n=185)). Patient demographics, ET cycle information and obstetrical outcomes are shown in Table 1. In the FET group, patients were significantly older (34.1 vs. 35.6, $p<0.005$) with a significantly greater number utilizing PGS (60.5% vs. 19.6%, $p<0.0001$). Significantly more women underwent FET induced labor (36.8% vs. 25.4%, $p<0.05$) and birthweight was significantly

increased compared to fresh ET (3357.5 vs. 3122.9g, p<0.005). Patients utilizing a fresh ET had significantly increased endometrial thickness at transfer (9.7 vs. 9.1mm, p<0.05). Infants were born at similar gestational ages between groups with similar rates of adverse perinatal outcomes. There was no significant difference in the rate of cesarean section and operative delivery. Fresh ET patients were considered small for gestational age (SGA) more often than FET patients, based on growth sonograms at 24 and 32 weeks' gestation. Controlling for cycle type, for every increase in estradiol of 1pg/ml there was a corresponding decrease in birthweight of 0.085g (p=0.0005). Estradiol level and endometrial thickness at transfer did not significantly impact gestational age at delivery or the chance of developing preeclampsia or gestational diabetes.

Conclusions:

Despite the increased patient age in the FET group, both fresh and frozen SET cycles resulted in low rates of adverse obstetrical outcomes, with similar incidence of preeclampsia, gestational diabetes, and low birth weight. FET cycles resulted in significant increases in birthweight without increasing rates of infants born LGA or via operative or cesarean delivery. Furthermore, FET cycles were not associated with increased risk of abnormal placentation or macrosomia. Estradiol levels at ET were inversely correlated with birthweight, consistent with the notion that supraphysiologic hormone levels may lead to impaired placentation and affect fetal growth. In an era of routine PGT and FET cycles, patients can expect improved placentation, as evidence by increased birthweight and the ability to perform embryo screening without incurring additional risk of adverse perinatal outcomes.

Support:

None

Table 1:

	Fresh SET	Frozen SET	P value
Live births	138	185	--
Age	34.1 ± 4.8	35.6 ± 4.4	0.0041
BMI	23.3 ± 4.0	22.6 ± 3.5	NS
Parity	0.4 ± 0.6	0.6 ± 0.7	0.0423
Pregnancy weight gain (lbs)	38.4 ± 48.2	43.6 ± 47.6	NS
Endometrial thickness at ET (mm)	9.7 ± 2.3	9.1 ± 1.9	0.0303
E2 at surge (pg/ml)	2730.5 ± 1358.9	573.5 ± 502.6	<0.0001
Trophectoderm	19.6% (27/138)	60.5% (112/185)	<0.0001

biopsied			
Gestational hypertension	8.7% (12/138)	8.1% (15/185)	NS
Severe preeclampsia	5.1% (7/138)	3.2% (6/185)	NS
1 hour glucose tolerance test	110.9 ± 28.8	111.8 ± 28.5	NS
Gestational diabetes	6.5% (9/138)	3.8% (7/185)	NS
Anatomy scan cervical length (cm)	4.5 ± 0.9	4.4 ± 0.7	NS
Small for gestational age (<10%) (SGA) at 24 weeks	3.6% (5/138)	1.6% (3/185)	NS
SGA at 32 weeks	1.4% (2/138)	0% (0/185)	NS
Head to abdominal circumference ratio	1.2 ± 0.05	1.2 ± 0.05	NS
Placenta previa	4.3% (6/138)	1.6% (3/185)	NS
Gestational age at delivery (weeks)	38.6 ± 2.5	38.5 ± 4.2	NS
Preterm delivery (<37 weeks)	13.0% (18/138)	11.4% (21/185)	NS
Infant gender ratio (M:F)	79:59	100:85	NS
Birthweight (g)	3122.9 ± 632.2	3357.5 ± 580.9	0.0008
Low Birthweight (<2500g)	9.4% (13/138)	8.1% (15/185)	NS
Macrosomia (>4500g)	0.7% (1/138)	0.1% (2/185)	NS
Labor Induction	25.4% (35/138)	36.8% (68/185)	0.03
Cesarean section delivery	47.1% (65/138)	52.9% (98/185)	NS
Operative delivery	4.3% (6/138)	6.5% (12/185)	NS