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Title:
Does Fresh Embryo Transfer Accentuate the Perinatal Risks of Dichorionic Twin Gestations?

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Objective:
Twins are at higher risk for fetal growth restriction and stillbirth compared to singleton gestations. Dichorionic twins, conceived spontaneously or by IVF, often have discordant growth as a consequence defective trophoblast invasion or impaired development of uteroplacental circulation. Significant birthweight (BW) discordance is associated with poor perinatal outcome. Recently, controlled ovarian hyperstimulation (COH) followed by fresh embryo transfer (ET) has been linked to defective placentation, evidenced by lower BW compared to pregnancies conceived from frozen embryo transfer (FET). While this notion has been demonstrated in studies of singleton gestations, there is limited data examining the effect of ovarian stimulation on growth and prematurity in twin gestations.

Design:
Retrospective cohort study

Materials and Methods:
All fresh or frozen ET cycles in which patients had ≥2 blastocysts transferred from November 2002 to July 2015, resulting in live twin birth at≥24 weeks gestation, were included. Cycles with spontaneously/selectively reduced twin gestations were excluded. Main outcome measures included gestational age at delivery, twin BW, BW discordance and the incidence of prematurity and poor growth (low/very low/extremely low BW). Student's t-test, chi-square and linear regression analysis were used.

Results:
Nine hundred and fifty eight patients delivered dichorionic twins after fresh (n=772) and frozen ETs (n=186). Patient demographics, cycle characteristics and perinatal outcomes are listed in

Table 1. Fresh ET twins had a significantly lower mean average BW (2127.8g vs. 2314.8g, <0.005) than the FET group. For every 1pg/ml increase in peak estradiol there was a 0.06g decrease in the averaged twin BW (<0.0001). The degree of BW discordance and prematurity were similar among groups.

Conclusions:

Similar to what is reported in singleton pregnancies, dichorionic twins conceived after fresh ET had lower BW compared with their FET cohort. However, the adverse effects on proper trophoblast invasion and placentation appeared to be mild as they did not translate into increased BW discordance, prematurity or BW <2500g. Further studies incorporating additional perinatal outcomes (ie. preeclampsia) are required to better understand the role of the endometrial hormonal milieu on placentation.

Support:

None

Table:

	Twins from fresh ET	Twins from frozen-thawed ET	P value
Total cycles	772	186	
Patient's age at ET	33.4 ± 4.0	33.3 ± 3.9	NS
BMI	24.5 ± 5.0	23.9 ± 4.1	NS
Day 3 FSH	5.5 ± 3.2	5.8 ± 2.3	NS
Endometrial Thickness at transfer (mm)	11.7 ± 3.2	10.3 ± 6.1	NS
Peak E2	3415.0 ± 1580.9	648.4 ± 564.5	NS
Number of Embryos Transferred	2.2 ± 0.5	2.2 ± 0.5	NS
Gestational age at delivery (wks)	34.8 ± 2.5	34.8 ± 2.5	NS
Late preterm delivery (35-37 wks)	40.9% (316/772)	47.3% (88/186)	NS
Early preterm delivery (24-34 wks)	38.9% (300/772)	38.2% (71/186)	NS
Length at birth (average of twins) (cm)	18.3 ± 1.5	18.3 ± 1.7	NS
Mean averaged birthweight of twins (g) Mean birthweight of smaller twin Mean birthweight of larger twin	2127.8 ± 841.1 1973.85 ± 836.0 2281.8 ± 886.3	2314.8 ± 673.5 2159.4 ± 672.9 2470.3 ± 710.9	<0.005 <0.005 <0.005
Mean birthweight difference among twins (g)	304.2 ± 281.7	306.8 ± 253.8	NS
Birthweight discordance	11.9%	11.8%	NS
>=1 twin with low birthweight (<2500g)	66.5% (513/772)	65.1% (121/186	NS
>=1 twin with very low birthweight (<1500g)	10.4% (80/772)	8.6% (16/186)	NS
>=1 twin with extreme low birthweight (<1000g)	3.0% (23/772)	2.7% (5/186)	NS
>=1 twin with macrosomia (>4500g)	0.1% (1/772)	0.0% (0/186)	NS