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Title:

Are Early Morphokinectic Parameters Predictive of Monozygotic Splitting After Single Embryo Transfer (SET)?

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Objective:
Extended in vitro culture has improved the ability to select the optimal embryo for transfer from both a genomic and morphokinetic perspective, though some have suggested that the delay in transferring embryos back to the uterus may be a risk factor for monozygotic twinning (MZT). Due to its rare incidence and IVF's longstanding practice to return multiple embryos at transfer, a clear link between blastocyst morphology and MZT has yet to be demonstrated. Since MZT gestations confer additional perinatal morbidity and mortality, we undertook this study to assess whether early morphokinetic findings were correlated with monozygotic twinning.

Design:
Case control study.

Materials and Methods:
All singleton and MZT clinical pregnancies from single, euploid frozen-thawed embryo transfers (FET) from July 2011 to April 2016 were included. All embryos underwent cleavage stage assisted hatching and day 5 FET. FETs were stratified by day of trophectoderm (TE) biopsy and blastocyst morphology (expansion, inner cell mass (ICM) and TE grade). Student's t-test, chi-square, linear and binary logistic regression analysis were performed.

Results:
Six hundred forty-five clinical pregnancies from 1238 FETs were eligible for the study's analysis. Baseline demographics and FET cycle characteristics are shown in Table 1. The incidence of monozygotic twinning was 3.7% (n=24). The odds of monozygotic splitting was not influenced by endometrial thickness at transfer (OR 0.94 [95% CI 0.6-1.4], p=0.79), peak estrogen level (OR 1.0 [95% CI 0.99-1.0], p=0.86) or the day of blastocyst biopsy (x2=0.003,

p=0.96). No association between MZT and blastocyst expansion (x2=0.38, p=0.94), ICM (x2=2.4, p=0.49) or TE (x2=1.7, p=0.63) was observed.

Conclusions:

Controlling for the number of embryos transferred, the endometrial environment and laboratory manipulation of the preimplantation blastocyst, the incidence of monozygotic splitting was neither correlated with expansion, inner cell mass grade, nor trophectoderm score. Further research is required to examine the potential influence of laboratory procedures, such as assisted hatching and trophectoderm biopsy, on the odds of MZT. Furthermore, the use of time-lapse technology may be informative regarding the mechanism underlying early splitting, in vitro.

Support:

None

Table 1:

	Singletons (n=621)	Monozygotic twins (n=24)	P value
Patient age at ET	36.6 ± 4.2	36.5 ± 4.6	NS
Oocyte age	35.8 ± 4.2	35.3 ± 5.1	NS
BMI at ET	23.0 ± 4.0	22.1 ± 3.9	NS
Day 3 FSH	6.2 ± 3.4	5.1 ± 3.1	NS
Endometrial Thickness at ET (mm)	9.2 ± 2.0	9.3 ± 2.5	NS
Peak E_2	544.7 ± 455.7	561.2 ± 452.1	NS
Day 5 biopsy	61.2% (380/621)	70.8% (17/24)	NS
Day 6 biopsy	38.8% (241/621)	29.2% (7/24)	NS
Blastocyst expansion grade=4	35.0% (217/620)	29.2% (7/24)	NS
Blastocyst expansion grade=5	28.4% (176/620)	29.2% (7/24)	NS
Blastocyst expansion grade=6	36.6% (227/620)	41.7% (10/24)	NS
Inner Cell Mass grade=A	75.5% (458/607)	70.8% (17/24)	NS
Inner Cell Mass grade=B	21.7% (132/607)	20.8% (5/24)	NS
Inner Cell Mass grade=C	2.8% (17/607)	8.3% (2/24)	NS
Trophectoderm grade=A	35.3% (214/607)	25.0% (6/24)	NS
Trophectoderm grade=B	48.6% (295/607)	62.5% (15/24)	NS
Trophectoderm grade=C	16.1% (98/607)	12.5% (3/24)	NS