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Title:

Are Reproductively Competent Blastocysts With Poor Morphological Grade at an Increased Risk for Adverse Perinatal Outcome?

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Objective:
Single embryo transfer (SET) is an increasingly being utilized to reduce the incidence of multiple gestations in IVF. Embryo selection can be optimized by morphological grading and preimplantation genetic screening (PGS) to select embryos with the best reproductive potential for transfer. While morphology is strongly correlated with implantation potential, it is not known whether poor morphology that implant result in defective placentation, and thus to impaired fetal growth and/or preterm delivery. This study sought to assess whether there is an association between embryo morphokinetics and perinatal outcome.

Design:
Retrospective cohort and case control study.

Materials and Methods:
All patients who achieved a singleton live birth after a frozen-thawed SET from May 2003 to July 2015 were included. Monozygotic twins were excluded from the analysis. Cycles were stratified based on the Gardner-Schoolcraft grading system for blastocyst expansion (BE), inner cell mass (ICM) and trophectoderm (TE). BE grade ≤3 (n=10) were excluded. Patient age, BMI, endometrial thickness at transfer, gestational age at delivery and neonatal birthweight were recorded. Student's t-test, chi-square and linear regression were used for analysis. Patients were stratified into birthweight categories (low birthweight (LBW) and macrosomia) and a binary logistic regression was used to identify whether morphokinetic factors were predictive of either outcome.

Results:
A total of 420 frozen SET cycles resulting in a live singleton birth were identified. There was no difference in patient age, BMI, endometrial thickness at transfer, gestational age at delivery or

infant birthweight among the morphological grading categories for BE, ICM or TE. A significantly higher proportion of day 5 embryo transfers in expansion 4 vs. 5 and 6 groups were observed. Controlling for this, birthweight was not influenced by the grade of expansion (p=0.5), ICM (p=0.4) or TE (p=0.9). However, the odds of LBW (<2500g) was significantly increased for expansion grade 4 (OR 4.7 [95% CI 1.3-30.0], p=0.04) and 5 (OR 5.2 [95% CI 1.3-34.9], p=0.04) blastocysts compared with 6 (Table 1). TE (x2=0.8, p=0.7) and ICM (x2=0.9, p=0.6) grade did not influence the occurrence of LBW. Morphological grade of BE, ICM and TE did not significantly influence the odds of macrosomia or preterm delivery.

Conclusions:

Patients can be reassured that transfer of an embryo deemed "poor quality" by morphologic grading is not associated with a decrease in gestational age at delivery or infant birthweight. While the overall incidence of LBW deliveries was low across all morphokinetic cohorts, we identified a preponderance of LBW singletons after transfer of a less expanded blastocyst. While the use of frozen-thawed embryos enables maximal synchronization between embryonic and endometrial development, it is possible that less expanded, slower developing blastocysts are slightly asynchronous with endometrial receptivity, leading to defective placentation and decreased fetal growth in patients with an underlying susceptibility.

Support:

None

Table 1:

Blastocyst expansion grade	4	5	6	P value
Number of patients	198	96	116	
Age	35.3 ± 4.6	35.3 ± 4.1	36.4 ± 3.7	NS
BMI	22.8 ± 3.8	22.7 ± 3.2	23.1 ± 4.0	NS
Endometrial thickness at ET (mm)	9.5 ± 2.1	9.3 ± 2.3	9.3 ± 1.8	NS
Day 5 blastocyst	52.0% (103/198)*	30.2% (29/96)	27.6% (32/116)	<0.05
Day 6 blastocyst	47.0% (93/198)*	69.8% (67/96)	72.4% (84/116)	<0.05
Gestational age at delivery (weeks)	37.9 ± 2.4	38.0 ± 1.9	40.7 ± 26.5	NS
Preterm delivery (<37 weeks)	19.7% (39/198)	20.4% (20/98)	14.7% (17/116)	NS
Birthweight (g)	3320.5 ± 622.0	3312.8 ± 617.3	3387.2 ± 497.7	NS
Low Birthweight (<2500g)	7.6% (15/198)	8.3% (8/96)	1.7% (2/116)*	<0.05

Macrosomia (>4500g)	0.5% (1/198)	3.1% (3/96)	0.9% (1/116)	NS

*denotes the parameters with a significant difference