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Title:

EVALUATING IVF AND PERINATAL OUTCOMES FOLLOWING REPEAT TROPHECTODERM BIOPSY

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Objective:

Trophectoderm biopsy (TB) and preimplantation genetic testing (PGT) enable the identification and selection of euploid embryos for transfer. Occasionally, PGT is limited by failed DNA amplification, data inconsistency, or other technical limitations, resulting in a non-diagnostic result. In these situations, patients must choose whether to have these embryos warmed and transferred "unscreened," or rebiopsied and reanalyzed, and depending upon the results, then transferred in a subsequent cycle. While the safety of blastocyst vitrification and TB has been widely demonstrated in both the literature and clinical practice, there is a paucity of data regarding the impact of repeated TB. Furthermore, it is not known whether repeat TB could have downstream effects on placentation. The purpose of our study was to evaluate whether repeat TB has an impact on IVF and perinatal outcome, while controlling for the effects of double vitrification-warming.

Design:

Retrospective, cohort study

Materials and Methods:

Patients who underwent euploid frozen embryo transfer (FET) of blastocysts that underwent double or single TB from October 2013 to March 2018 were included in the analysis. Quantitative polymerase chain reaction (PCR), array comparative genomic hybridization (aCGH), and targeted next generation sequencing (NGS) were used to perform preimplantation genetic testing (PGT). Patients were grouped by the number of TBs performed during treatment. The double TB group underwent transfer of a euploid frozen-thawed blastocyst after warming, rebiopsy and re-vitrification due to a non-diagnostic PGT result after initial TB. The single TB group had previously vitrified unscreened embryos that were warmed, biopsied once and re-vitrified, prior to FET. The baseline demographics, cycle characteristics, and outcomes were compared between groups. IVF outcomes included implantation, ongoing pregnancy, early pregnancy loss (EPL), and live birth. Perinatal outcomes included gestational age, infant birthweight, and the rates of preterm delivery and low birth weight. Student's t-test, chi-square, linear and binary logistic regression analysis were performed.

Result(s):

Eighty-one patients whose embryos underwent double TB to obtain definitive PGT results prior to ET were compared to 56 controls. Baseline demographics, FET cycle characteristics and outcomes are shown in Table 1. Controlling for oocyte age, BMI, endometrial thickness, hatching status, and day of biopsy, the odds of ongoing pregnancy was reduced in the double TB group (OR 0.37 [95% CI 0.15-0.95], p=0.0382). The odds of EPL were not modified by double TE biopsy (OR 3.49 [95% CI 0.77-15.8], p=0.11). Controlling for age, gestational age at delivery was not impacted by the number of TB biopsies (b= 0.70, p=0.21). Controlling for age and gestational age at delivery, double TB biopsy did not significantly impact infant birthweight (b= -144.2, p=0.39).

Conclusion(s):

While repeat embryo vitrification and thawing can be safely performed in the modern IVF laboratory, our findings suggest that performance of a second TB may decrease blastocyst implantation potential. Once pregnancy is established, patients that undergo transfer of double biopsied blastocysts can be reassured that they are not at increased risk of pregnancy loss, preterm delivery or reduced infant birthweight. As the capability of PGT technology expands, patients may request that their embryos undergo repeat testing for conditions for which these embryos were not originally tested, warranting further studies to confirm our findings. Our study design allowed us to isolate the effect of repeat TB, by controlling for embryo exposure to double vitrification and warming. While there appears to be a 15% decrease in implantation rate for vitrified embryos that undergo rewarming, biopsy, and refreezing, this risk must be balanced against the potential benefits gained from obtaining a clinically impactful PGT diagnosis.

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References:

None

Table 1:

	Single TB	Double TB	p value
Patient age at ET	35.4 ± 4.1 (23.5-43.9)	36.8 ± 4.1 (25.3-44.6)	0.0626
Oocyte age	32.9 ± 4.1 (23.1-40.0)	36.1 ± 4.1 (25.1-42.9)	<0.0001
BMI at ET	22.6 ± 3.8	24.0 ± 4.9	0.0641
Endometrial thickness at ET (mm)	9.3 ± 1.9	9.7 ± 2.2	0.3797
Proportion of embryos that underwent first TE biopsy on day 5	42.9% (24/56)	53.1% (43/81)	0.239
Proportion of embryos that underwent first TE biopsy on day 6	50.0% (28/56)	43.2% (35/81)	0.433
Proportion of embryos that underwent first TE biopsy on day 7	7.1% (4/56)	3.7% (3/81)	0.369
Proportion of hatched (expansion grade 6) embryos	25.0% (14/56)	51.9% (42/81)	0.001673
Implantation rate	66.1% (37/56)	40.7% (33/81)	0.003548
Ongoing pregnancy rate	62.5% (35/56)	35.8% (29/81)	0.002077
Early pregnancy loss rate	7.5% (3/40)	18.2% (8/44)	0.14723
Live birth rate	45.9% (17/37)	31.0% (13/42)	0.1706
Gestational age at delivery	37.8 ± 1.7	38.5 ± 1.1	0.2027
Preterm delivery rate	11.8% (2/17)	7.7% (1/13)	0.8923
Infant birthweight	3400.2 ± 524.6	3365.1 ± 378.5	0.8562

Low birthweight	5.9% (1/17)	0.0% (0/13)	0.392804