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Title:

DIRECT CORRELATION BETWEEN B-HCG LEVELS AND TROPHECTODERM MORPHOLOGY QUALITY IN SINGLE EUPLOID EMBRYO TRANSFER CYCLES

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Objective:

Embryonic trophectoderm (TE) cells play a key role in apposition, adhesion, and invasion of the maternal endometrium during early implantation. Blastocysts are morphologically graded (expansion stage (EXP); inner cell mass (ICM); trophectoderm (TE) cells) to better understand embryonic competence and improve selection at transfer. Data is scarce regarding the relationship of embryo TE quality and early levels of β-hCG, a biochemical marker of early embryo implantation and placentation. Previously, we demonstrated that embryo TE quality does not correlate with major adverse perinatal outcomes or placental weight at delivery. However, patients who had transfer of embryo(s) with a low TE grade experienced placental histological changes. (Herlihy et al. 2017) This study included patients who underwent a single, euploid frozen embryo transfer (FET) and assessed the correlation between embryo TE grade and early β-hCG levels.

Design:

Retrospective cohort analysis

Materials and Methods:

This study included patients who underwent a single, euploid FET cycle and obtained a positive pregnancy test (serum β-hCG ≥5 mIU/mL) from 2015 to 2019. The β-hCG measurement was analyzed 9 days after FET using an electrochemiluminescence immunoassays (Immulite 2000; Siemmens and/or Cobas e-601; Roche). Only cases that had a first β-hCG measurement on day 9 after ET were included in the analysis. Blastocyst morphology was assessed using a center-specific, modified Gardner's scoring system. ANOVA, χi2 tests, univariate, multivariate linear regression and a mixed effects model with a random intercept model were used to evaluate serum β-hCG levels with regard to TE grade.

Results:

A total of 2,954 single, euploid FET cycles were included in the analysis. Cohorts were segregated by TE grade: (TE-A: n=1,076; TE-B: n=1,235; TE-C: n=643). β-hCG values were significantly different among cohorts (TE-A: 155.5±97; TE-B: 133.7±80; TE-C: 94.1±73, p=<0.0001) and early pregnancy loss (EPL) was significantly higher in embryos with low TE grades: (TE-A:14.6%, TE-B:15.3%, TE-C: 19.2%, p=0.01) There was a significant correlation between TE grade and mean β-hCG levels (R2: 0.06, p<0.001). After adjusting for age, BMI, endometrial thickness at ET, ICM grade, EXP grade, and day of embryo biopsy, the correlation between high TE grade and high β-HCG levels remained significant (R2:0.12, P=<0.0001).

Conclusion:

After adjusting for clinical parameters, embryonic expansion, and inner cell mass grade; our data showed euploid embryo TE grade correlates with β-hCG levels at first pregnancy test measurement. The ultrastructural appearance of the TE cells in euploid embryos might represent a surrogate marker of embryo's capacity to properly adhere and invade the endometrium during the early implantation process. Further studies focusing on syncytiotrophoblast and endometrial cellular and molecular interactions could help reproductive specialists to better understand the mechanisms related to early placentation physiology.