THE PREDICTIVE VALUE OF ESTRADIOL LEVEL FOR PREGNANCY OUTCOMES IN EUPLOID NATURAL CYCLE FROZEN EMBRYO TRANFERS

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Objective: To determine whether estradiol (E2) level on the day of LH surge/hCG trigger in euploid natural cycle frozen embryo transfers (NC-FET) is associated with pregnancy outcomes

Design: IRB-approved retrospective cohort study

Materials and Methods: All NC-FET with euploid blastocysts performed at a single academic institution from May 2016 to March 2019 were reviewed. Demographic data including age, BMI, parity, race, smoking status, and SART diagnosis were collected. All patients underwent uterine cavity evaluation with correction if needed prior to NC-FET. Standard protocol for NC-FET included hCG trigger when the dominant follicle was ≥18 mm and the endometrial lining was ≥7 mm. NC-FET was performed 6 days after spontaneous LH surge (augmented with hCG trigger) or 7 days after hCG trigger alone. E2 (pg/mL) was evaluated on the day of hCG trigger. Vaginal progesterone was started 3 days before NC-FET. NC-FET with E2 <200 were compared to NC-FET with E2 ≥200. The primary outcomes of interest were clinical pregnancy rate (CPR, defined as intrauterine gestation with positive fetal cardiac activity) and live birth rate (LBR). *The R Project for Statistical Computing* was used to complete independent t-tests for continuous variables, chi-square tests for categorical variables, and logistic regressions for outcome variables.

Results: A total of 441 NC-FET were analyzed. Mean age at transfer was 36.5 ±SD 3.8 years, and mean BMI was 25.0 ±SD 4.8 kg/m^2. The majority of patients were nulliparous (63%), Asian (51%) or White (39%), and never smokers (95%). Mean E2 on the day of spontaneous LH surge/hCG trigger was 274 ±SD 121. The overall CPR was 65%, and the overall LBR was 61%. There were 134 NC-FET with E2 <200 and 307 NC-FET with E2 ≥200. Demographic variables did not significantly differ between the 2 groups, except for mean BMI, which was 26.2 in the E2 <200 group vs. 24.4 in the E2 ≥200 group, p<0.01. CPR was 58% for cycles with E2 <200 vs. 68% for cycles with E2 ≥200, p=0.04; LBR was 52% for cycles with E2 <200 vs. 65% for cycles with E2 ≥200, p=0.01. In a logistic regression controlling for age at transfer, BMI, parity, race, smoking status, endometrial thickness, and embryo grade, E2 ≥200 still predicted an increased CPR (OR 1.74 [CI 1.11, 2.72]) and an increased LBR (OR 1.94 [CI 1.25, 3.03]).

Conclusions: The focus before proceeding with NC-FET has traditionally been dominant follicle size and endometrial thickness. E2 level may also play an important role in preparing the endometrium for implantation and pregnancy, as suggested by a study of 101 untested, cleavage-stage NC-FET (1). The strength of our study lies in its larger cohort size and inclusion of only euploid blastocysts. In our patient population, E2 ≥200 at the time of hCG trigger in NC-FET predicted an increased CPR and LBR, both with statistical significance. These findings support delaying hCG trigger if E2 <200 in the absence of an LH surge, even when criteria for dominant follicle size and endometrial thickness are met. When an LH

surge occurs and delaying hCG trigger is not possible, providers may consider postponing NC-FET to another cycle when E2 might be more optimal.

Reference:

1. Ramezanali, F, et al. Serum estradiol level on trigger day impacts clinical pregnancy rate in modified natural frozen embryo transfer cycles. Int J Gynaecol Obstet. 2019 Jun;145(3):312-8.