OPTIMIZING THE MODIFIED NATURAL FROZEN EMBRYO TRANSFER PROTOCOL: SHOULD WE WAIT FOR AN ENDOGENOUS LUTEINIZING HORMONE SURGE?

Authors: Yamada R (1), Genovese H (2), Willson S (2), Whitehead C (2), Drews M (2), Werner M (2)

Affiliations: (1) Rutgers Robert Wood Johnson Medical School, Department of Obstetrics, Gynecology, and Reproductive Sciences, New Brunswick, NJ, USA; and (2) IVIRMA New Jersey, Basking Ridge, NJ, USA

Background
Modified natural frozen embryo transfer (FET) cycles are commonly utilized; however, it is unclear if an endogenous luteinizing hormone (LH) surge is advantageous in comparison to the LH surge achieved after an exogenous human chorionic gonadotropin (hCG) trigger.
Objective
This study examines pregnancy outcomes in modified natural FET cycles that utilize exogenous hCG trigger prior to the detection of an endogenous LH surge—based on follicle size alone—in comparison to cycles with an endogenous LH surge present in conjunction with appropriate follicular size.
Materials and Methods
This is a retrospective cohort study of patients at an academic-affiliated private practice from 2012 to 2021. Included patients were undergoing their first FET cycle using a modified natural protocol with transfer of a single frozen euploid blastocyst. Gestational carriers and patients with a thin endometrial lining <7 mm were excluded. Patients who had an endogenous LH surge (defined as an LH value ≥20 IU/L) prior to exogenous hCG trigger were classified into the "surge" group, while those who were triggered based on the size of the dominant follicle alone were classified into the "no surge" group. The primary outcome was sustained implantation rate (SIR), defined as ongoing intrauterine pregnancy at 8 weeks gestation. Secondary outcomes were clinical pregnancy rate (CPR), loss, live birth rate (LBR), preterm birth (PTB), and low birth weight <2500 grams (LBW). Data analysis was performed with Pearson's Chi-Squared test and logistic regression analysis after controlling for body mass index (BMI), oocyte age, and embryo grade.
Results
There were 1014 patients included (N=239 in the "surge" group, N=775 in the "no surge" group). Patients with an endogenous surge were triggered one day earlier on average (mean cycle day 12.95 vs 13.74, p=0.002). SIR was not significantly different between the "surge" and "no surge" groups (72.0% vs 68.4% [OR 1.20, 95% CI 0.87-1.67]). Additionally, there were no differences in CPR (78.7% vs 74.5% [OR 1.25, 95% CI 0.87-1.77]), loss (13.4% vs 13.8% [OR 0.92, 95% CI 0.60-1.42]), LBR (70.3% vs 67.7% [OR 1.14, 95% CI 0.82-1.57]), PTB (5.9% vs 4.0% [OR 1.47, 95% CI 0.75-2.88]), or LBW (7.7% vs 6.4% [OR 1.29, 95% CI 0.65-2.58]). A secondary analysis was done within the "surge" group to more stringently define an endogenous surge as an LH rise with a concurrent progesterone rise of ≥1.0 ng/mL (N=53) and ≥1.2 ng/mL (N=23) six days prior to FET. In the subgroup analyses for both progesterone levels, there was no statistical difference in SIR (p=0.64, p=0.84), LBR (p=0.68, p=0.66), or PTB (p=0.94, p=0.60).
Conclusions
In modified natural FET cycles, SIR, LBR, PTB, and LBW are not influenced by the presence of an endogenous LH surge prior to administration of hCG trigger. A prospective study on endogenous LH rise that includes daily measurements of LH, progesterone, and estradiol may be useful in defining the most optimal protocol.
Financial Support
None