INCIDENCE AND ZYGOSITY OF MULTIPLE BIRTHS FOLLOWING A NATURAL OR PROGRAMMED SINGLE FROZEN BLASTOCYST TRANSFER CYCLE

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Abstract Text:

BACKGROUND: The use of single Frozen Embryo Transfers (sFETs) has led to a virtual elimination of multiple pregnancies. In some cases, however, transferring a frozen embryo in a natural cycle can lead to twins from the frozen embryo transfer due to a natural ovulation. **OBJECTIVE:** The objective of this study is to compare the incidence and zygosity of twins and higher order multiples in modified natural compared to programmed sFETs, so as to facilitate appropriate counseling of patients regarding the importance of abstinence during natural and semi-natural sFET cycles.

MATERIALS AND METHODS: Retrospective cohort study of sFET twin and higher-order multiples pregnancies from U.S.-based Boston IVF clinics. Deidentified data was extracted from a single electronic medical record database (eIVF). Medical records from August 2013 to April 2024 were reviewed. Patients of maternal age 18-43 who underwent an autologous sFET cycle and had a confirmed twin or higher-order multiple pregnancy were included in final analysis. The type of twin pregnancy was confirmed by reviewing seven-week OB ultrasound and physician notes in patient charts. Comparisons were made using the chi-square test for categorical variables and parametric OR non-parametric tests for continuous variables based on data distribution. GEE model clustered by patient was used (to account for the correlation of patients that had more than 1 transfer cycle) to predict the outcomes. All tests were two sided and a P value <0.05 was required to confer significance

RESULTS: 283 patients were included in the final analysis. There was a significant difference in the likelihood of pregnancies leading to two or more fetuses in the natural cycle group vs. programmed (p = 0.045, chi-squared = 4.01). Using OR analyses, the odds of achieving twins or higher-order multiples are lower for programmed compared to natural cycles (OR=0.59, CI 95% (0.36-0.96)). These findings were consistent when adjusting for age at transfer and number of fetal sacs. Further research is needed to confirm that the higher rate of twins/multiples in the natural cycle group is due to concurrent natural conception.

CONCLUSIONS: sFETs have the goal of a singleton pregnancy for patients undergoing ART treatments for infertility. There is an unavoidable risk of monozygotic twinning, occurring at frequency of about 2%¹. Patients who have intercourse during their natural sFET cycle may also be at risk of having a fraternal twin (or multiples) conception^{1,2}. The data show that the incidence of twins and higher-order multiples is significantly higher in natural cycle compared to programmed cycle sFETs. With this data, providers can facilitate appropriate counseling of patients regarding the importance of abstinence during natural and semi-natural sFET cycles to mitigate the risks that come with multiple gestations.

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REFERENCES:

 Mateizel I, Santos-Ribeiro S, Done E, et al. Do ARTs affect the incidence of monozygotic twinning? Hum Reprod. 2016;31(11):2435-2441. doi:10.1093/humrep/dew216 Vaughan DA, Seidler EA, Murphy LA, et al. Double trouble? Clinic-specific risk factors for monozygotic twinning. Fertil Steril. 2020;114(3):587-594. doi:10.1016/j.fertnstert.2020.04.010