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Title

Frozen-thawed Embryo Transfers in Natural Ovulation Cycles Have Lower Miscarriage Rates than Hormone Replacement Cycles

Introduction

Hormone replacement cycles (HRC) are more commonly used than natural ovulation cycles (NC) for frozen-thawed embryo transfers. In recent years, NC has been reconsidered due to concerns about perinatal complications, but no consensus has been reached regarding early pregnancy outcomes. In this study, we compared HRC and NC, focusing on miscarriage rates.

Methods

From 2020 to 2022, we retrospectively examined the patient characteristics, clinical pregnancy rates, and miscarriage rates of 6,138 patients who underwent 11,623 cycles of frozen-thawed embryo transfers at three facilities in our group. The data were obtained from medical records. For statistical analysis, we used the chi-square test and multivariate analysis.

Results

There were 7,822 cycles for HRC and 3,801 cycles for NC. No significant differences were observed in patient characteristics such as average age, endometrial thickness, history of delivery, history of miscarriage, BMI, and AMH levels. The clinical pregnancy rate, indicated by the presence of a gestational sac (GS), was 36.6% in HRC and 37.6% in NC, with no significant difference between the two groups. However, the

miscarriage rate after GS confirmation was 25.3% in HRC and 21.1% in NC ($P < 0.05$). A significant difference in miscarriage rates was also observed among patients over 40 years old, with rates of 38.9% in HRC and 32.4% in NC ($P < 0.05$). A similar trend was observed in euploid blastocyst transfers after preimplantation genetic testing for aneuploidy (PGT-A) (HRC: 143 cycles, NC: 100 cycles). In a multivariate analysis of miscarriage rates after GS confirmation, HRC was identified as a significant factor, along with age, cleavage-stage embryo transfers, and non-PGT-A.

Conclusions

Although pregnancy rates are similar between HRC and NC, the miscarriage rate is significantly lower in NC. This suggests that differences in endometrial preparation methods used in frozen-thawed embryo transfers may affect outcomes. NC may be the preferred method for endometrial preparation in cases where spontaneous ovulation can be expected.