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Title:

DOES EXTENDING CONTROLLED OVARIAN HYPERSTIMULATION DURING A GNRH ANTAGONIST PROTOCOL IN VITRO FERTILIZATION CYCLE AFFECT OOCYTE QUALITY?

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Objective:

The number of oocytes retrieved during an in vitro fertilization (IVF) cycle is an important determinant of success. Timing of the oocyte maturation trigger during controlled ovarian hyperstimulation (COH) must be optimized to maximize oocyte yield while avoiding hyperstimulation syndrome and impaired oocyte quality. A common protocol prescribes trigger administration when ≥ 2 follicles reach ≥ 18 mm. Periodically, clinicians delay the trigger to allow medium-size follicles to “catch up.” A recent study segregated 200 IVF cycles into groups: delayed trigger despite the ≥ 2 mature follicles and trigger administration with ≥ 2 mature follicles, and found no difference in clinical pregnancy rate (CPR) and live birth rate (LBR). The clinicians transferred 1-2 fresh, unscreened embryos, which limits generalizability. To eliminate confounders such as multi-embryo transfer and the effect of supraphysiologic hormone levels on the endometrium, we asked whether rates of oocyte maturation, fertilization, blastulation, and euploidy were affected by prolonging COH.

Design:

Retrospective, cohort study

Materials and Methods:



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The study included patients at a single academic center who underwent GnRH-antagonist IVF cycles from 2012-19. Cycles were grouped: (1) delayed trigger despite the presence ≥ 2 mature follicles, and (2) administration of trigger in the presence of ≥ 2 mature follicles. Primary outcome was oocyte metaphase II (MII) rate. Secondary outcomes were rates of fertilization, blastulation, and euploidy. Statistical analysis was performed with T-tests, chi-square tests, and multivariate logistic regressions.

Results:

Of the 7,976 antagonist IVF cycles from 6,478 patients, trigger was administered in the presence of ≥ 2 mature follicles in 6521 (81.8%) cycles, 1 day beyond in 1334 (16.7%) cycles, and 2 days beyond in 121 (1.5%) cycles. Univariate analysis demonstrated differences in age, antral follicle count, peak estradiol, gravidity, and trigger type. After controlling for these confounders, no significant association was observed for continuing COH beyond visualization of ≥ 2 mature follicles and MII rate (OR 1.01 [95% CI 0.90-1.13]), fertilization rate (OR 0.98 [95% CI 0.88-1.10]), blastulation rate (OR 0.97 [95% CI 0.87-1.08]), or euploidy rate (OR 0.90 [95% CI 0.78-1.04]). A sub-analysis was performed for SART age group E, which also showed no differences in cycle outcomes when COH was extended.

Conclusion:

In the largest study of GnRH antagonist protocol IVF cycles looking at oocyte developmental competence when trigger was delayed in the presence of ≥ 2 mature follicles, we demonstrated no significant difference in rates of maturation, fertilization, blastulation, and euploidy, even in patients >42 years old. Our study suggests that continuing COH up to 2 days in select patients does not negatively affect outcomes. While reassuring, the effects of COH prolongation on genomic and non-genomic factors must be investigated. Well-controlled prospective studies assessing CPR and LBR will be needed before we can definitively quantify the limits around optimal COH duration.