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EFFICACY OF SERUM FOLLICLE-STIMULATING HORMONE LEVEL MONITORING DURING LETROZOLE-GONADOTROPIN OVARIAN STIMULATION CYCLES. J. Kim,[a,b] V. Turan,[a,b] G. Bedoschi,[a,b] K. Oktay.[a,b] [a]New York Medical College, Valhalla, NY; [b]Innovation Institute for Fertility Preservation and IVF, New York, NY.

OBJECTIVE: To investigate the feasibility and efficacy of monitoring serum follicle–stimulating hormone (FSH) levels during letrozole-FSH ovarian stimulation cycles for fertility preservation (FP).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: One-hundred and thirty eight women diagnosed with stage ≤3 breast cancer, who underwent ovarian stimulation with a letrozole-FSH protocol for FP were included. Serum FSH levels were measured throughout the cycle monitoring. Stimulation outcomes such as number of total and mature oocytes retrieved were recorded.

RESULTS: The multivariate analysis revealed that serum FSH levels both on 5th day of stimulation (FSH-5) and trigger day (FSH-t) had significant inverse relationship with number of total oocytes ($p=0.008$ and $p<0.0001$) and mature oocytes ($p=0.04$ and $p<0.0001$) retrieved after adjusting age, body weight and FSH dose administered. The risk of OHSS (>15 total oocytes) was significantly higher when FSH-5 ≤22 mIU/mL (OR:14.3,;95% CI:2.5, 81.4) and FSH-t≤23mIU/mL (OR:5.3; 95% CI:1.8, 16.0). When FSH-t was greater than 26 mIU/mL, the risk of poor response (<5 oocytes or <4 mature oocytes) was significantly higher (OR:3.7 (95% CI: 1.4, 10.1)

TABLE 1. OR for poor response and high risk of OHSS at calculated cut-off values from ROC analysis

Poor response	High risk of OHSS
Day 5 FSH > 32 mIU/ml - OR (95% CI): 5.2[a] (0.8 - 34.1)	Day 5 FSH ≤ 22 mIU/ml - OR (95% CI): 14.3[a] (2.5 - 81.4)
Trigger Day FSH > 26 mIU/ml - OR (95% CI): 3.7[b] (1.4 - 10.1)	Trigger Day FSH ≤ 23 mIU/ml - OR (95% CI): 5.3[b] (1.8 - 16.0)

[a]Adjusted for age at stimulation, weight and starting FSH dose. [b]Adjusted for age at stimulation, weight and total FSH dose.

CONCLUSION: Serum FSH level monitoring may improve safety margin of ovarian stimulation. Serum FSH on the 5th and trigger day of stimulation may be predictive of oocyte retrieval outcomes. The additional information gained from serum FSH monitoring may enhance outcomes in FP cycles using letrozole and FSH.

Supported by: NIH RO1 HD053112 and R21 HD061259.

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THE USE OF A "DOUBLE TRIGGER" FOR FERTILITY PRESERVATION IN POOR RESPONDERS. F. S. Pacheco,[a,b] A. Small,[b] C. Acosta,[a] K. Acosta,[a] S. Dunn,[a] K. Oktay.[a,b] [a]Innovation Fertility Preservation & IVF, New York, NY; [b]New York Medical College, Valhalla, NY.

OBJECTIVE: In the practice of fertility preservation, poor responder patients present a special challenge, as often there is no time for repeated cycles. It is therefore crucial to investigate methods to improve mature oocyte yield from every follicle. Our objective was to test a "double-trigger" approach to determine if oocyte maturity and D-3 embryo development can be improved in this population of patients.

DESIGN: Retrospective.

MATERIALS AND METHODS: Seventeen cycles from 6 women undergoing fertility preservation for various indications were deemed poor responders based on the Bologna criteria[1]. All were stimulated with FSH (300-450 IU) with or without letrozole 5 mg added throughout. A GnRH antagonist was given when the lead follicle diameter reached ≥13 mm, and when the same reached ≥17-mm, hCG (1000 IU - 2500 IU) and leuprolide acetate (40-80 IU) were given 30-34 hours before retrieval. Trigger day was influenced by the follicle cohort, length of stimulation and in one case, cancer treatment start date. LH surge was confirmed next morning. During retrieval, each follicle was aspirated separately to identify the association of size with oocyte maturity. Those that were M-II were either vitrified (2 patients, 3cycles) or subjected to ICSI (4 patients, 14 cycles) and cryopreserved on D-3 stage.

RESULTS: From the 17 cycles, 40/74 follicles were ≤13 mm on the trigger day. These yielded 47 oocytes of which 38 were mature (72%). 13 mature oocytes originated from follicles ≤13mm , resulting in 62% (13/21) maturity rate. This was compared to the maturity rate of 96% (25/26) from follicles ≥13-mm ($p=0.003$). Strikingly, 8 MII oocytes were retrieved from follicles ≤10 mm (62% MII rate), showing a similar maturity rate to those 10-13 mm follicles. Of those MII, 7 were cryopreserved and remaining were ICSIed resulting in the cryopreservation of 27 D3-embryos (D3 embryo rate=87%). Of the 9 immature oocytes, 8 came from follicles ≤13-mm, 2 matured in vitro, further increasing the total mature oocyte yield to 71.4% for follicles ≤13 mm.

CONCLUSION: We presented novel evidence that mature oocytes can be obtained from very small follicles. The double trigger approach described here maybe helpful in improving mature oocyte yield from small follicles in poor responders and possibly when there is insufficient time to perform a full-length ovarian stimulation.

Supported by: NIH R01 HD053112; R21 HD061259

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CO –TRANSPLANTATION OF OVARIAN TISSUE WITH ENDOTHELIAL CELLS FOR REDUCTION OF GRAFT ISCHEMIA. L. Man, D. Reichman, K. Chao, Z. Rosenwaks, G. Schattman, D. James. The Ronald O. Perelman & Claudia Cohen Center for Reproductive Medicine, Weill-Cornell Medical College, New York, NY.

OBJECTIVE: Graft ischemia due to suboptimal revascularization is a major hurdle towards implementation of efficient ovarian cryopreservation in clinical practice. Endothelial cells (ECs) exhibit unique paracrine signals that foster tissue regeneration and revascularization; co-engrafting ovarian-specific ECs with ovarian tissue in heterotopic locations may greatly foster viability, maximizing outcomes.

DESIGN: Murine ovarian tissue transplantation model.

MATERIALS AND METHODS: Ovaries from RFP (red fluorescent protein) mice were engrafted into age-matched, oophorectomized VEGFR2-GFP (Vascular endothelial growth factor receptor 2) recipients, in which endothelial cells fluoresce green; ovaries from VEGFR2-GFP mice were engrafted into oophorectomized RFP mice to assess the origin of new vessels (host versus graft). Tissue-specific ECs were isolated from adult mice, expanded in vitro, and labeled with a third fluorescent protein (Crimson) using lentiviral transduction. Wild-type B6 mouse ovaries (10-12 wk old) were transplanted into flanks of oophorectomized WT recipient B6 mice with co-transplantation of GFP-labeled ECs. Each mouse served as its own control, with a contralateral engraftment site without ECs. Engrafted tissue was harvested at multiple time points (1–4 weeks) and assessed for contribution of exogenous, host and graft-derived ECs to the transplant as well as degree of functional revascularization (lectin perfusion) in EC-adjuvant versus control engraftment sites. Histologic sections were analyzed using confocal microscopy.

RESULTS: Graft revascularization occurred in both directions, with new vessels arising in the graft originating from the host, and new vessels in the host originating from the graft. Ovarian transplants with co-transplantation of ECs exhibited robust engraftment. Exogenous GFP-labeled ECs were present throughout the area of transplantation, within ovarian stroma, and, notably, in theca and granulosa cell layers of the follicles themselves.

CONCLUSION: Exogenous ECs contribute to neovascularization and reperfusion of transplanted ovary. Further study is warranted to determine whether organ-specific subtypes of ECs preferentially benefit engrafted tissue. Moreover, genetically modified ECs engineered to secrete specific paracrine factors will establish a novel platform to test factors that foster or hinder optimal engraftment and, more broadly, to interrogate molecular influences that affect follicle viability, recruitment, and maturation.

Supported by: Entirely internal (CRMI funding).