New Approach May Boost Success of IVF

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FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE

DENVER – A bolus of follicle stimulating hormone given at the time of the human chorionic gonadotropin trigger during in vitro fertilization improves the developmental competence of oocytes, a new randomized trial shows.

The result is improved oocyte recovery, a higher fertilization rate, and perhaps a higher pregnancy rate, Dr. Julie D. Lamb said at the meeting.

"These findings may change our current practice, and with further study may play a pivotal role in improving ART outcomes for our patients," according to Dr. Lamb of the University of California, San Francisco.

She presented a double-blind clinical trial in which 188 IVF patients undergoing a long agonist suppression protocol were randomized to a 450-IU bolus of FSH or placebo at the time of hCG trigger, 36 hours before oocyte retrieval.

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Major Finding: The measure of fertility rate, consisting of the number of normal fertilized oocytes divided by the total number of oocytes collected, was 63% in the group given an FSH bolus as compared to 55% with placebo, a significant difference. The fertility rate in IVF cycles was 62% with FSH bolus and 48% in controls. In cycles involving intracytoplasmic sperm injection, the rates were 79% with FSH and 73% in controls.

Data Source: A double-blind clinical trial in which 188 IVF patients undergoing a long agonist suppression protocol were randomized to a 450-IU bolus of FSH or placebo at the time of hCG trigger, 36 hours before oocyte retrieval.

Disclosures: Dr. Lamb disclosed having received a research grant from Ferring Pharmaceuticals.

The study rationale was that spontaneous ovulation in most mammalian species is preceded by a surge in FSH and luteinizing hormone, a combined gonadotropin surge believed necessary to final oocyte maturation and follicular rupture.

However, in modern stimulation protocols the last dose of FSH is often given 2 days prior to egg retrieval, and with intentional pituitary suppression little endogenous FSH is present at the pivotal time.

The study hypothesis was that creating a more physiologic ovulation trigger process would improve the developmental competence of oocytes.

"The dramatically increased success in IVF in the last two decades has been attributed largely to improvement in the embryo culture, laboratory conditions, and optimization of different stimulation protocols. Less attention has been given to different methods of hCG induction of final oocyte maturation," she said.

The study results indicate this is a fruitful new area. The primary outcome – a measure of fertility rate consisting of the number of normal fertilized oocytes divided by the total number of oocytes collected – was 63% in the FSH group compared with 55% with placebo, a significant difference. The FSH bolus improved the fertility rate in IVF cycles, where it was 62% compared with 48% in controls, but not in cycles involving intracytoplasmic sperm injection, where the rates were 79% with FSH and similar at 73% in controls.

Turning to secondary end points, Dr. Lamb reported that the oocyte recovery rate – the chance of obtaining an oocyte upon flushing or aspirating a mature follicle – was 70% in the FSH group, significantly better than the 57% with placebo.

The implantation rate was 40% in the FSH group compared with 35% in the placebo arm. Clinical pregnancy as defined by fetal heart motion on ultrasound occurred in 57% of women in the FSH group compared with 46% of controls. The composite rate of ongoing pregnancy beyond 24 weeks or live birth was 51% in the FSH group and 43% in

controls. None of these differences were statistically significant. However, the trends consistently favored the FSH intervention. Since the study wasn't powered to show significant differences in pregnancy outcomes, a larger trial will be required to determine whether the FSH bolus truly does boost pregnancy rates, Dr. Lamb said.

Follicular fluid FSH levels on the day of oocyte retrieval were significantly higher in the bolus FSH recipients at 13.3 mIU/mL compared with 9.2 mIU/mL, confirming that the supplemental FSH reached the follicular fluid. The benefits of bolus FSH weren't due to a change in the broader intrafollicular hormone milieu, since follicular fluid levels of testosterone, estradiol, progesterone, and hCG were similar in the two study arms.

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DR. LAMB

No cases of ovarian hyperstimulation syndrome occurred with the study protocol because women with a baseline estradiol level greater than 4,500 pg/mL were excluded from participation as a precautionary measure.

Dr. Lamb said the next step planned by the researchers is a dose-finding study to learn whether a smaller dose of FSH would be equally effective, or if perhaps a larger dose would bring a better response.

She disclosed having received a research grant from Ferring Pharmaceuticals. ■