Medical Xpress

Elective freezing of IVF embryos linked to higher pregnancy rates in some cases

August 1 2017

A delay in transferring embryos to the mother improves the success of in vitro fertilization in certain cases, according to a study by scientists at the Stanford University School of Medicine, Celmatix Inc. and several other institutions.

Women undergoing IVF who have high levels of the hormone progesterone when their egg cells are retrieved benefit from having the resulting embryos frozen and transferred back to the uterus at a later date, the researchers found.

The study appears in the August issue of *Fertility and Sterility*. The lead author is Ange Wang, MD, a resident physician in obstetrics and gynecology at Stanford. Several other co-authors, including senior author Piraye Yurttas Beim, PhD, work for Celmatix, a company that makes software and a genetic test to help guide fertility treatments for women.

The IVF process starts with injections of reproductive hormones to stimulate the growth of multiple eggs. The eggs are retrieved and then fertilized in the laboratory. The resulting embryos can be transferred back to the woman's uterus a few days later (a "fresh" transfer) or frozen and then transferred in a subsequent hormonal cycle.

The new study, which analyzed 2,910 attempts to establish pregnancy via IVF, is the largest ever to compare frozen with fresh embryo transfer. Given that the highest-quality embryos are typically transferred to a woman first and that the scientists wanted to diminish the possible

influence of embryo quality on the results, IVF procedures in which a woman had "leftover" frozen embryos transferred following a failed fresh transfer were not included in the study.

The greatest difference between the frozen and fresh procedures was seen in women who had high progesterone levels and were older than 35. For these women, freezing the embryos before transfer was 73 percent more likely to produce an ongoing pregnancy than transferring the embryos immediately after IVF.

"This finding is important because it may suggest a group of women that benefits more from freeze-all IVF cycles," Wang said. In freeze-all cycles, all embryos are frozen for later transfer. "Higher progesterone levels may make it more difficult for embryos to implant—that is, adhere to the wall of the uterus to establish pregnancy—possibly due to premature maturation of the uterine lining," Wang said.

The researchers speculated that freezing embryos and waiting to transfer them during a different cycle gives an opportunity for progesterone and other hormones to fall to levels more hospitable to implantation, although this idea was not directly tested.

The database the researchers used included information about implantation rates and also about which IVF cycles led to pregnancies lasting long enough for patients to be transferred from the care of fertility centers to regular obstetric practices, reported in the study as "ongoing pregnancy." Live birth data were not reported.

Common approach

Freezing embryos created during IVF before transferring them back to the patient has become increasingly common as freezing techniques have improved. Tests to examine embryos for chromosomal or genetic

diseases are also becoming more widely used, and these often require freezing. But physicians have been unsure whether transferring frozen embryos changed pregnancy rates. Until now, only small studies have been done, and some have been inconclusive.

To compare success rates of transferring fresh versus frozen embryos, Wang and her colleagues used a large database maintained by Celmatix that contains records of hundreds of thousands of IVF treatments performed at 12 fertility treatment centers in the United States. From the database, two cohorts of 1,455 IVF transfers were selected to study: one group in which all the embryos were frozen before transfer, and another group in which fresh embryos were transferred. Patients in the two cohorts had similar ages, causes of infertility, reproductive histories, numbers of eggs retrieved, number of embryos created and levels of reproductive hormones.

A 73 percent higher pregnancy rate

Fifty-two percent of the embryo transfers performed after embryos were frozen led to ongoing pregnancies, whereas 45.3 percent of fresh transfers led to ongoing pregnancies. After analyzing all IVF transfers together, the researchers performed separate comparisons of women with lower and higher progesterone levels, as well as of women who were younger and older than 35. Women with lower progesterone levels who received previously frozen embryos did not experience better pregnancy outcomes, regardless of their age. However, among women with higher progesterone levels at the time of egg retrieval, transferring previously frozen embryos resulted in more pregnancies both in younger and older patients. The difference was greatest in patients with high progesterone levels who were older than 35. In this group, 48.4 percent of transfers using previously frozen embryos resulted in pregnancies, compared with 35.2 percent of fresh transfers. In other words, for older women with high progesterone levels, the odds of pregnancy were 73

percent greater following transfer of previously frozen embryos.

The new findings may prompt physicians to suggest that patients with high progesterone levels at egg retrieval freeze their embryos and wait for a subsequent cycle to transfer them, said Wang. But other factors also influence the decision about which protocol to use, she said.

"If I were counseling an IVF patient on whether to choose a freeze-all cycle, it would depend on the characteristics of her cycle, as well as her own desires," Wang said. "Though this data suggests promising effects of freeze-all transfers, it is still important to listen to patients' preferences. Some women do not want to wait to transfer embryos or have financial or other considerations that may impact their choice."

Provided by Stanford University Medical Center

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