

Study, Metaanalysis Show Vitrification Superior

BY KATE JOHNSON
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NEW ORLEANS — A prospective, randomized comparison of two oocyte cryopreservation methods suggests vitrification may be superior to the older slow-freeze technique, Gary D. Smith, Ph.D., reported at the annual meeting of the American Society for Reproductive Medicine.

His results are backed up by a metaanalytic comparison of both methods performed by Dr. Kutluk Oktay from Cornell University, Ithaca, N.Y., and also reported at the meeting. “Your paper is what this field was lacking,” Dr. Oktay told Dr. Smith. “It is these types of studies that will tell us the real story.”

As interest in egg freezing has intensified—both for medical and social indications—so too has the debate about which cryopreservation method is best.

Dr. Smith’s preliminary findings from 37 frozen oocyte cycles suggest that vitrification results in better fertilization, cleavage, and biochemical pregnancy rates per thaw, compared with slow freezing. “Whether this translates to a better live birth rate remains to be seen,” said Dr. Smith, director of the gamete cryopreservation laboratory at the University of Michigan, Ann Arbor, who conducted the study in collaboration with Huntington Center for Reproductive Medicine of Brazil, in São Paulo.

The study included women undergoing fresh in vitro fertilization who desired cryopreservation of oocytes instead of embryos. A total of 114 women were randomized to freeze oocytes either by slow freezing or vitrification. There have been 37 thaw cycles to date: 17 from the vitrification group and 20 from the slow-freezing group, he reported. Postthaw survival was not interrupted significantly differently between the two groups; however,

fertilization and cleavage were significantly better in the vitrification group (73% and 85%, respectively), compared with the slow-freeze group (57% and 70%, respectively), he said. In addition, the biochemical pregnancy rate per transfer was higher in the vitrification group (62%), compared with the slow-freeze group (22%), although this difference did not reach significance because of the small numbers. Similarly, there were more ongoing and live births per thaw in the vitrification group (44%), compared with the slow-freeze group (22%), but again, numbers were too small to establish significance.

Dr. Oktay’s metaanalysis also suggested the superiority of vitrification over slow freezing. The metaanalysis included studies using either egg-freezing technique and compared their results with success rates for fresh intracytoplasmic sperm injection (ICSI), reported his research fellow, Dr. Aylin Cil, at the meeting.

After excluding studies that did not use ICSI, used immature oocytes, or had missing data, the meta-analysis revealed a total of 214 clinical pregnancies and 159 live births reported from cryopreserved oocytes. Live births per transfer were significantly better in studies using vitrification (37%), compared with slow freezing (16%), although the mean number of embryos transferred was significantly higher in the vitrification group (3.5 vs. 2.5) and the multiple pregnancy rate was also higher (28% vs. 19%). “Supernumerary embryo transfer may at least partially be responsible for the higher success rates with vitrification,” reported Dr. Cil. The mean age of patients also was lower in the vitrification studies (32.3 vs. 33.7).

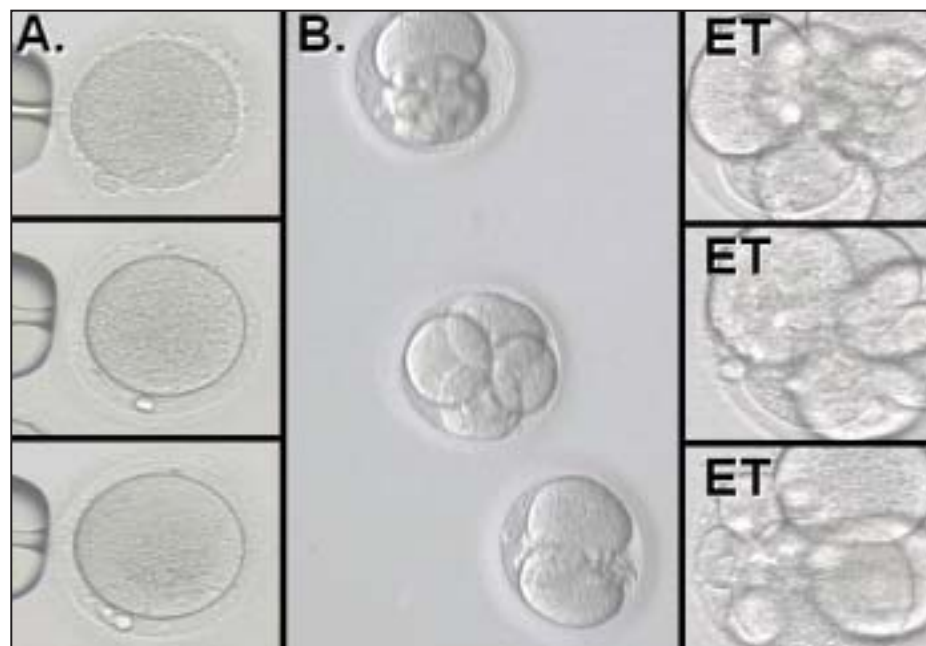
When comparing either egg freezing technique to fresh ICSI results reported by the Society for Assisted Reproductive Technology, the metaanalysis found similar live birth rates per transfer in vitrifica-

tion and fresh ICSI (37% and 44%, respectively, a difference that was not statistically significant) in women of the same age. However, slow-freeze results were significantly lower than fresh results in the respective age groups (16% vs. 38%).

“The body of evidence is pointing toward vitrification as the superior method but there is still no definitive study,” commented Dr. Jamie Grifo, director of the division of reproductive endocrinology and infertility at New York University, New York. “The metaanalysis has many limitations and the other study needs more numbers to be definitive.” Dr. Grifo’s group also presented a study at the meeting in which 14 infertile patients underwent 15 cycles of egg freezing/thawing and subsequent embryo transfer. All but one of the patients had some eggs vitrified and others slow frozen. To date, there have been six deliveries of eight babies, all healthy, he reported. All but one of the pregnancies resulted from a mixed transfer of embryos derived from both vitrified and slow-frozen eggs.

“It is unclear from this study which cryopreservation method, if any, is superior—we didn’t have enough data to answer this question,” Dr. Grifo said in an interview. “We are currently designing a trial where patients are randomized to either method, but the power analysis requires about 45 cycles to have statistically significant data.”

However, he said the important point is that egg freezing can produce results that are comparable with fresh cycles. “We have an ongoing/delivered pregnancy rate of 47% and an implantation rate of 36%. ... The playing field between men and women with regard to fertility preservation has been leveled,” he said. “It is hoped that using this technique in cancer patients or patients wishing to preserve fertility by choice will yield even higher success rates than the infertile population included in our study.”



Three human oocytes have been vitrified, warmed, and cultured (A). Embryos are shown 2 days after ICSI (B). Embryos are shown on day 3 of embryo transfer (ET).

PHOTOS COURTESY DR. GARY D. SMITH

Screen Tags IVF Patients Who May Have Trouble With Failure

BY KATE JOHNSON
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NEW ORLEANS — The majority of women who are at risk for anxiety and depression following a failed in vitro fertilization cycle can be identified by a one-page screening questionnaire administered before treatment, Christianne M. Verhaak, Ph.D., reported at the annual meeting of the American Society for Reproductive Medicine.

“If you can identify who is at risk before the start of treatment, you can offer them tailored intervention in time to prevent future emotional problems,” said Dr. Verhaak, a clinical psychologist at Radboud University Nijmegen Medical Center in the Netherlands.

She suggested that simply informing patients about the emo-

tional impact of unsuccessful treatment can help them prepare appropriately. “For most patients and their families, the emotional impact of infertility is unknown because it is still not easy for people to talk about,” she said in an interview. “But it is comparable to grief. With grief, people expect an emotional reaction, they understand that is not something that passes after 1 or 2 months—it’s something that takes a lot of time and often involves a reconsideration of one’s life.”

Her study, which was awarded the Mental Health Professional Group prize paper at the meeting, followed 400 women who were starting in vitro fertilization (IVF) cycles at eight different fertility clinics in the Netherlands. Psychological questionnaires were administered before treatment, after each IVF cycle, and 6

months after the last IVF cycle. The questionnaires included the short version Spielberger State Trait Anxiety Inventory (STAI) to assess state anxiety, the Beck Depression Inventory (BDI) to assess depression, the Illness cognition questionnaire to assess cognitions of helplessness and acceptance regarding infertility, and a social support inventory.

Six months after the end of all IVF treatment, 20% of the women who had failed to become pregnant showed clinically relevant levels of anxiety and 25% showed clinically relevant levels of depression, reported Dr. Verhaak. “What is important is that in these women no recovery had taken place since the end of treatment. A negative response to treatment failure is normal, but in grief studies, recovery is apparent by 6 months, and if it is

absent this is considered abnormal.” She added that emotional problems that interfere with daily life are almost always associated with failed, rather than successful, IVF cycles.

“The emotional impact is mostly influenced by the stress of possible childlessness. So if the treatment succeeds, in most cases the stress diminishes considerably,” Dr. Verhaak said.

The study found five pretreatment risk factors that were associated with persistent emotional problems after treatment: anxiety, depression, cognitions of helplessness, reduced cognitions of acceptance, and lack of social support. Patients with at least one of these risk factors had a fourfold chance of developing posttreatment emotional problems compared with patients who had no risk factors, she said.

The researchers then developed a one-page screening tool to identify these risk factors before treatment and validated the tool in a separate group of 512 patients. They found the screening tool identified 74% of the overall cohort correctly as either at risk or not, with a sensitivity of 69% and a specificity of 79%. The sensitivity increased to 70% and the specificity to 87% in the subgroup of women who did not get pregnant.

Dr. Verhaak said the findings suggest that screening all patients is worthwhile before they start IVF; this would include both those with primary and those with secondary infertility. “The longing for a second child is the same as the longing for a first child, and the emotional impact of not getting pregnant is the same in both cases,” she said.