Study, Metaanalysis Show Vitrification Superior

BY KATE JOHNSON
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New Orleans — A prospective, ran- domized comparison of both cryo- preservation methods suggests vitrifica- tion 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 metaan- alytic comparison of both methods per- formed by Dr. Kurtluk 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 intensi- fied—both for medical and social indica- tions—as to too hard the debate about which cryopreservation method is best.

Dr. Smith’s preliminary findings from 37 frozen oocyte cycles suggest that vitrifi- cation results in better fertilization, cleav- age, 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 cryopreser- vation 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 cryo- preservation of oocytes instead of em- bryos. A total of 114 women were ran- domized to freeze oocytes either by slow freezing or vitrification. There have been 37 thaw cycles to date: 17 from the vitri- fication group and 20 from the slow-freez- ing group, he reported. Post thaw survival was not interrupted significantly differ- ently between the two groups; however, fertilization and cleavage were significant- ly better in the vitrification group (73% and 85%, respectively), compared with the slow-freeze group (77% and 70%, respec- tively), said Dr. Smith. In addition, the biochemical pregnancy rate per transfer was higher in the vitrification group (62%), compared with the slow-freeze group (22%), al- though this difference did not reach sig- nificance 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 stud- ies using either egg-freezing technique and compared their results with success rates for fresh intracytoplasmic sperm injec- tion (ICSI), reported his research fellow, Dr. Ailyn Cil, at the meeting.

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).

After excluding studies that did not use ICSI, used immature oocytes, or had missing data, the meta-analysis revealed a to- tal of 214 clinical pregnancies and 199 live births reported from cryopreserved oocytes. Live births per transfer were sig- nificantly better in studies using vitrifica- tion (37%), compared with slow freezing (16%), although the mean number of em- bryos transferred was significantly higher in the vitrification group (3.5 vs. 2.5) and the multiple pregnancy rate was also high- er (28% vs. 19%). “Supernumerary em- bryo transfer may at least partially be re- sponsible for the higher success rates with vitrification,” reported Dr. Cil. The mean age of patients also was lower in the vitrifica- tion 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 simi- lar live birth rates per transfer in vitrifica- tion and fresh ICSI (37% and 44%, re- spectively, a difference that was not statisti- cally significant) in women of the same age. However, slow freeze results were significantly lower than those in the respective age groups (16% vs. 38%).

“The body of evidence is pointing to- ward vitrification as the superior method but there is still no definitive study,” com- mented Dr. Jamie Grifo, director of the di- vision of reproductive endocrinology and infertility at New York University, New York. “The metaanalysis has many limita- tions and the other study needs more numbers to be definitive.” Dr. Grifo’s group also presented a study at the meet- ing in which 14 infertile patients under- went 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 14 deliveries of eight babies, all healthy, he reported. All but one of the pregnancies resulted from a mixed trans- fer of embryos derived from both vitrified and slow-frozen eggs.

“It is unclear from this study which cryo- preservation 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 46% ... The playing field between men and women with regard to fertility preserva- tion has been leveled,” he said. “It is hoped that using this technique in cancer patients will enable women to preserve fertility by choice will yield even higher success rates than the infertility population included in our study.”

Screen Tags IVF Patients Who May Have Trouble With Failure

BY KATE JOHNSON
Montreal Bureau

New Orleans — The majority of women who are at risk for anxiety and depression fol- lowing a failed in vitro fertiliza- tion cycle can be identified by a one-page screening questionnaire administered before treatment, Christiane M. Verhaak, Ph.D., reported at the annual meeting of the American Society for Repro- ductive Medicine.

“If you can identify who is at risk before the start of treatment, you can offer them tailored in- terventions that may help with future emotional problems,” said Dr. Verhaak, a clinical psycholo- gist at Radboud University Nij- megen Medical Center in the Netherlands.

She suggested that simply in- forming 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 peo- ple to talk about,” she said in an interview. “It is difficult to talk about failure. With grief, people expect an emotional reaction, they un- derstand that is not something that passes after 1 or 2 months—it’s something that takes a lot of time and often involves a recon- sideration of one’s life.”

Her study, which was awarded the Mental Health Professional Group paper at the meet- ing, followed 400 women who were starting in vitro fertiliza- tion (IVF) cycles at eight different fertility clinics in the Netherlands. Psychological questionnaires were administered before treat- ment, 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 cog- nition 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 be- come pregnant showed clinically relevant levels of anxiety and 27% 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.”

The negative response to treatment failure is normal, but in grief studies, recovery is ap- parent by 6 months, and if it is absent this is considered abnor- mal.” She added that emotional problems that interfere with dai- ly life are almost always associ- ated with failed, rather than suc- cessful, IVF cycles.

“The emotional impact is mostly influenced by the stress of possible childlessness. So if the treatment succeeds, in most cas- es the stress diminishes consider- ably,” Dr. Verhaak said.

Her study found five treat- ment risk factors that were asso- ciated with persistent emotional problems after treatment: anx- iety, 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 prob- lems compared with patients who had no risk factors, she said.

The researchers then devel- oped a one-page screening tool to identify these risk factors before treatment and validated the tool in a separate group of 512 pa- tients. They found the screening tool identified 74.2% of the overall cohort correctly as either at risk or not, with a sensitivity of 60% and a specificity of 79%. The sen- sitivity increased to 70% and the specificity to 87% in the sub- group of women who did not get pregnant.

Dr. Verhaak said the findings suggest that screening all patients is worthwhile before they start IVF. “We are still not convincing both those with primary and those with secondary infertility. ‘The longing for a second child is the same in the longings for a first child, and the emotional impact of not getting pregnant is the same in both cases,’ she said.”