

Vitrification May Be Viable Option for Oocytes

BY KATE JOHNSON

AMSTERDAM — Vitrified ovarian tissue yields a greater number of viable oocytes after thaw and transplant, compared with tissue that is frozen using conventional techniques, according to data presented at the European Society of Human Reproduction and Embryology.

“Both ischemic loss from cortical transplantation and oocyte loss from freezing can be prevented with ultrathin grafts and vitrification,” said Dr. Sherman Silber, director of the Infertility Center of St. Louis.

In fact, oocyte viability from transplanted vitrified ovarian tissue is similar to that of fresh transplants, he said.

In one study, Dr. Silber compared oocyte viability in 14 young cancer patients who had received ovarian tissue transplants after either vitrification (n = 8)

or conventional freezing (n = 6). He compared his results with those of nine patients who had received fresh ovarian tissue transplanted from their identical twins.

Oocyte viability was similar in the twin patients who had received fresh tissue and cancer patients who had received vitrified tissue, but was significantly decreased in cancer patients who had received conventionally frozen tissue, he reported.

“We found that 91.9% of the fresh oocytes were viable, compared with 88.9% of those vitrified. However, slow freezing resulted in a 56% loss of viability,” he said.

Ovarian function returned in all patients regardless of whether they had received fresh tissue or tissue frozen by either method, emphasized Dr. Silber. All patients regained a normal ovarian cycle 4-5 months after transplant.

Dr. Silber’s data point to the superiority of vitrification over conventional freezing, in terms of oocyte viability. However, another paper presented at the meeting suggests vitrification may re-



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sult in abnormal expression of a gene known as GAPDH (glyceraldehyde 3-phosphate dehydrogenase). In an in vitro study of human ovarian tissue, “we detected drastically reduced levels of GAPDH-gene expression in ovarian

tissue after vitrification, compared with conventional freezing,” reported Vladimir Isachenko, Ph.D., of the University of Ulm (Germany).

“This is a housekeeping gene,” he explained in an interview. “If there is no expression of this gene, or expression is decreased, it will eventually result in cell death,” he said.

Studies to date show no indication of abnormalities in children conceived from vitrified ovarian tissue or oocytes, commented Dr. Silber.

But abnormal gene expression could have very subtle effects that might also not become evident until adulthood, Dr. Isachenko explained. He suggested that the mechanism by which vitrification might alter gene expression might be the direct contact of tissue with liquid nitrogen. Based on his findings, his laboratory no longer uses vitrification. ■

Drugs for Inhibiting Uterine Contractions After IVF Studied

BY KATE JOHNSON

AMSTERDAM — Two drugs that inhibit uterine contractions might provide a novel approach to improving implantation rates in patients undergoing IVF, according to early research reported at the annual meeting of the European Society of Human Reproduction and Embryology.

“Contractions of the uterus are more frequent in IVF cycles compared to normal menstrual cycles, and a higher frequency of contractions around the time of embryo transfer is associated with a more negative impact on pregnancy outcomes,” reported Dr. Christophe Blockeel of the center for reproductive medicine, Universitair Ziekenhuis Brussel, Brussels, Belgium.

“We’ve learned that uterine contractions are actually in many cases expelling somewhere between 15% to 50% of embryos after transfer,” commented Roger Pierson, Ph.D., a collaborator in the study, and professor of obstetrics, gynecology, and reproductive sciences at the University of Saskatchewan (Sask).

“Regardless of which catheter you use, or whether or not you use ultrasound, you are still irritating the uterus and it doesn’t matter how gentle you are, some women are going to respond with advanced uterine contractions,” he said in an interview.

The study, which was conducted in oocyte donors and was funded by Ferring Pharmaceuticals, examined the effect of the selective oxytocin antagonist barusiban and the mixed oxytocin/vasopressin antagonist atosiban versus placebo on luteal phase uterine contractions.

The study participants were 125 oocyte donors who had undergone controlled ovarian stimulation, oocyte retrieval, and luteal phase supplementation with progesterone.

Women were randomized to either barusiban (41 women, IV bolus 9 mg, IV infusion 2.16 mg/h); atosiban (42 women, IV bolus 6.75 mg, IV infusion 18 mg/h); or placebo on day 2 after oocyte retrieval.

Transvaginal ultrasounds lasting at least 5 minutes were obtained after retrieval on day 1, 14 times on day 2 (pretreatment, 8 times before mock embryo transfer, 3 times after mock embryo transfer, and 2 times post infusion), and on day 5.

With both medications, the frequency of uterine contractions remained stable during the first 2 days after retrieval, followed by a significant decrease noted in both treatment groups that lasted for about 3 hours.

“These medications are quite short acting, so they need to be administered an hour or two before transfer just to get the uterus settled to facilitate implantation,” explained Dr. Pierson, who is also a consultant for Ferring.

Without the control medication the frequency of uterine contractions can be as high as 6 or 7 per minute after embryo transfer, he said, adding that the ideal is somewhere around 1 to 1.5 contractions per minute.

“This is a very new approach to improving implantation and quite different,” he explained. While atosiban is already used to treat preterm labor, barusiban was specifically developed to treat uterine contractions in IVF, and another similar medication is being developed by the company.

“Both barusiban and atosiban are very well tolerated drugs; however, toxicology tests are still needed before we can use these drugs in patients undergoing embryo transfer rather than donors,” Dr. Blockeel said. Optimal dosing also needs further investigation. ■

Patch Ups Favorable Lipids In Comparison Study

BY NEIL OSTERWEIL

BOSTON — The route of hormonal contraceptive administration—transdermal or oral—does not make a difference in terms of the hormone’s effect on plasma lipids and lipoproteins, according to the findings of a randomized crossover trial.

In the study, women on either a standard or extended-release contraceptive patch had higher levels of HDL cholesterol and its constituent apolipoprotein A1 (ApoA1), compared with when they were taking oral contraceptives; however, the effects of patch and oral formulations on atherogenic lipoproteins were similar, Dr. Elizabeth Chan reported at a symposium sponsored by the International Atherosclerosis Society.

“Patch contraception results in 60% higher estrogen levels than oral contraception. It is the estrogen/progesterone ratio that determines the overall lipoprotein effects in hormonal contraception formulations,” according to Dr. Chan of the University of Washington division of cardiology in Seattle and her colleagues.

Thirty-five healthy premenopausal women had a 2-month phase-in period on an oral contraceptive (Ortho-Cyclen; 35 mcg ethinyl estradiol and 0.25 mg norgestimate) and were then randomly assigned in a three-way crossover design to 2 months on the oral contraceptive, a patch formulation (Ortho-Evra,

approximating a daily dose of 20 mcg ethinyl estradiol and 150 mcg norelgestromin), or an extended-release patch (Extended Ortho-Evra, 7-week patch application plus 1 week off). Investigators were blinded to treatment assignment.

A total of 31 women completed all three treatments and were available for the final analysis. Lipoprotein lev-

els were measured on the 21st day of the second month of each treatment cycle, corresponding to peak hormonal effect.

The investigators found that the use of the standard patch formulation resulted in significantly higher levels of the favorable lipids—HDL and ApoA1—compared with oral adminis-

tration. The extended patch also had a significantly greater effect on HDL and ApoA1, compared with the standard patch. But for all other lipid parameters—LDL, non-HDL cholesterol, apolipoprotein B, and triglycerides—there were no significant differences among the three contraceptive formulations.

“The higher HDL cholesterol and ApoA1 seen with patch contraception may involve differences in formulation and/or reverse cholesterol transport. These mechanisms require further study,” said the researchers, who reported no conflicts of interest related to the study supported by Ortho-McNeil, maker of the contraceptives tested. ■

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