Length of time of embryo storage does not negatively influence pregnancy rates after thawing and transfer

J.H. Check, D. Summers-Chase, W. Yuan, K. Swenson, D. Horwath

The University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School at Camden, Cooper Hospital/University Medical Center, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology & Infertility, Camden, NJ (USA)

Summary

Purpose: To determine if longer storage of embryos in a cryopreserved state negatively affects the chance of successful implantation following thawing and transfer. Methods: A retrospective cohort analysis of frozen-thawed embryos that had been donated to recipients. Four time periods were evaluated. Results: No significant decrease in pregnancy or implantation rates was found in the longest freezing group (≥ 6 years). In fact, if there was a trend, it was for improved pregnancy rates with longer storage. One of the successes was from embryos stored about 12 years. Conclusions: Hopefully these data and results from other IVF centers will influence those countries having a mandatory discarding policy to reconsider and lift these restrictions, especially to increase the pool of embryos available for donation.

Key words: Cryopreservation; Donated embryos; Length of freezing.

Introduction

Some countries have requirements that specify that frozen stored embryos be destroyed after a period of time. Donated frozen embryos are at a premium. Frequently a couple will hold on to their frozen embryos not sure if they may want another child in the future.

When couples are about to lose their embryos some of them are emotionally forced to attempt another pregnancy before desired or even have another child that they may not be sure they really wanted. Instead others would donate their embryos to an anonymous couple at a later date if they were not "emotionally" forced to transfer them back to themselves or for others, and by waiting until the last minute, it would be too late to consider donating them.

The objective of the present study was to determine if there is any given length of time of being in the frozen state that reduces the chance of implantation potential of these frozen/thawed embryos.

Materials and Methods

The study was a retrospective cohort analysis. Only frozen donated embryo transfers were included in the study. This allowed more uniformity of results, because length of time in storage was not necessarily related to successful fresh transfer, therefore biasing the data.

All embryos were cryopreserved either at the 2-pronuclear (PN) or multicell stage. A simplified freezing protocol was used on all embryos with slow-cooling in a BioCool alcohol bath freezer, and a one-step removal of the cryoprotectant 1,2-propanediol upon thawing [1].

Transfers were performed on day 3, and were preceded by assisted embryo hatching [2].

Revised manuscript accepted for publication February 12, 2010

Results

There did not appear to be any decrease in pregnancy or implantation rates with longer embryo storage time as seen in Table 1. Although none of the parameters reached clinical significance, there actually seemed to be a trend toward higher implantation rates, and lower spontaneous abortion rates, with longer storage times.

In the "greater than ten years stored" group, the two patients out of three who got pregnant both delivered healthy babies. One was a singleton produced from multicell embryos frozen for 10.8 years [3]. The other was a twin delivery from a mixed batch of 2PN and multicell embryos which had been stored for 11.8 years. There were no birth defects in any of the donated embryo deliveries other than a hernia.

Discussion

From the current data we can conclude that there is no decline in implantation potential of cryopreserved embryos as length of storage time increases, as also found by Machtinger *et al.* [4]. This information is useful in counseling donor embryo recipients who may be concerned about choosing batches of embryos which have been in storage for long periods of time, as well as patients wishing to donate who are afraid that their stored embryos are no longer viable.

Some patients are hesitant to choose embryos which have been stored for long periods of time since little information is available concerning their possible viability, including birth defects [5]. These recipients could be reassured by the present data. Since many countries now have legislation authorizing (or even requiring) IVF clinics to destroy embryos after three to five years, it is important to acquire more information on this topic so legislators and oversight agencies can make informed decisions regarding the potential ramifications of destroying embryos based on arbitrary time limits.

Table 1.— Effect of length of freezing on pregnancy and implantation rates following frozen embryo transfer.

	Clinical pregnancy rate	SAB rate (failure/ clinical preg.)	Implantation rate	Live/delivered pregnancy rate
< 2 years	40.6%	30.8%	13.7%	28.1%
•	(13/32)	(4/13)	(16/117)	(9/32)
2.0-3.9 years	40.7%	13.6%	16.0%	35.2%
•	(22/54)	(3/22)	(30/188)	(19/22)
4.0-5.9 years	42.0%	19.0%	20.1%	36.0%
-	(21/50)	(4/22)	(35/174)	(18/21)
≥ 6 years	47.8%	0.0%	23.8%	47.8%
-	(22/46)	(0/22)	(34/143)	(22/46)
p value				
(chi-square				
analysis)	.887	.071	.135	.325

SAB: spontaneous abortion.

References

[1] Baker A.F., Check J.H., Hourani C.L.: "Survival and pregnancy rates of pronuclear stage human embryos cryopreserved and thawed using a single step addition and removal of cryoprotectants". Hum Reprod. Update 2, (CD-ROM), 1997.

- [2] Check J.H., Hoover L., Nazari A., O'Shaughnessy A., Summers D.: "The effect of assisted hatching on pregnancy rates after frozen embryo transfer". Fertil. Steril., 1996, 65, 254.
 [3] Check M.L., Check J.H., Summers-Chase D.: "A successful preg-
- [3] Check M.L., Check J.H., Summers-Chase D.: "A successful pregnancy from zygotes cryopreserved for > 9 years: Case report". *Clin. Exp. Obstet. Gynecol.*, 2001, 28, 91.
- [4] Machtinger R., Dor J., Levron J., Mashiach S., Levran D., Seidman D.S.: "The effect of prolonged cryopreservation on embryo survival". *Gynecol. Endocrinol.*, 2002, 16, 293.
- [5] Wennerholm W.B.: "Cryopreservation of embryos and oocytes: obstetric outcome and health in children". *Hum. Reprod.*, 2000, 15 (suppl. 5), 18.

Address reprint requests to: J.H. CHECK, M.D., Ph.D. 7447 Old York Road Melrose Park, PA 19027 (USA) e-mail: laurie@ccivf.com