

Fertilization by intracytoplasmic sperm injection (ICSI) does not impair subsequent pregnancy outcome following frozen embryo transfer (ET) as determined by a large retrospective analysis

B. Katsoff, C. Wilson, J.H. Check, W. Yuan, D. Summers-Chase

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, N.J. (USA)

Summary

Purpose: To determine if fertilization by intracytoplasmic sperm injection (ICSI) adversely affects pregnancy outcome following frozen embryo transfer (ET). **Methods:** Retrospective analysis of frozen ETs where the oocytes were fertilized by conventional insemination vs ICSI was carried out. **Results:** No difference in pregnancy outcome was found in women up to age 42. There was a non-significant trend for lower pregnancy rates in women age 43 and older. **Conclusions:** In the largest series to date by far these data convincingly show that fertilization by ICSI does not impair outcome following frozen ET.

Key words: Intracytoplasmic sperm injection; Frozen embryo transfer; Pregnancy outcome.

Introduction

The research group that presented the gift of intracytoplasmic sperm injection (ICSI) to the world claimed that one negative effect of ICSI was that it adversely affected implantation when transferring frozen-thawed embryos [1, 2].

However subsequently other studies claimed adequate pregnancy rates following transfer of frozen embryos that were a result of ICSI [3, 4]. These studies were relatively small.

There is always the chance of bias when evaluating small series claiming opposite conclusions of a previous study. In vitro fertilization centers reaching the same conclusions as the original one are less likely to submit their findings because nothing new was found. Reviewers are more likely to accept a manuscript with opposite rather than similar conclusions even if the latter has fewer cases than the original one.

The aim of the present study was to compare retrospectively in the largest series to date the pregnancy outcome following transfer of frozen-thawed embryos that had been fertilized by either conventional oocyte insemination or ICSI.

Materials and Methods

A retrospective evaluation of frozen-thawed embryo transfers over a seven-year period was performed.

The data were stratified according to whether the oocytes were fertilized using conventional insemination or ICSI. The data were further evaluated according to the age of the woman

at the time of fertilization: Group A - ≤ 35 , Group B - 36-39, Group C - 40-42, Group D - ≥ 43 .

The embryos had been cryopreserved with a simplified freezing protocol using 1,2 propanediol as the cryoprotectant with a one-step removal of the cryoprotectant upon thawing [5].

Assisted embryo hatching was performed before the transfer which for this study was all conducted on day 3 [4]. Some of the embryos transferred had been twice frozen and thawed [6]. Some of the embryo transfers were derived from metaphase I or germinal vesicle stage embryos which had been cultured in vitro one extra day before ICSI was performed [7]. The pregnancy and implantation rates were all from day 3 embryo transfers.

Results

The clinical and delivered pregnancy rates and implantation rates following frozen ETs for ages 42 and under seemed quite comparable between conventional oocyte insemination and ICSI as seen in Table 1.

Though no significant difference was found in comparing women ≥ 43 , there may have been a trend for higher pregnancy rates with conventional insemination. Only a larger series could determine if this difference was from chance alone.

Counting all ages, the clinical pregnancy rate for frozen ETs with ICSI was 36.3% (482/1,369) and the delivered pregnancy rate was 30.9% (403/1,369). The comparative data for conventional insemination was 38.0% (351/923) clinical pregnancy rate and 32.9% (304/923) delivered pregnancy rate ($p = \text{NS}$).

The implantation rate for the four age groups combined for the ICSI group was 15.3% (709/4,556) ($p = \text{NS}$). The implantation rate for those having conventional insemination was 16.8% (530/3,137) ($p = \text{NS}$).

Table 1. — Pregnancy rates for frozen ETs – ICSI vs non-ICSI according to age.

	Frozen ETs with ICSI				Frozen ETs without ICSI			
	≤ 35	36-39	40-42	≥ 43	≤ 35	36-39	40-42	≥ 43
# transfer ≥ 2 embryos	816	354	138	61	545	231	101	46
# clinical pregnancies	335	109	32	6	241	74	25	11
% clinical pregnancy/transfer	41.1	30.8	23.2	9.8	44.2	32.0	24.8	23.9
# delivered	285	89	27	2	218	60	19	7
% delivered/transfer	34.9	25.1	19.6	3.3	40.0	26.0	18.8	15.2
# first trimester losses	74	25	8	5	33	19	8	6
% first trimester losses	22.1	22.9	25.0	83.3	13.7	25.7	32.0	54.5
# embryos transferred	2,560	1,245	533	218	1,776	816	389	156
Average # embryos transferred	3.1	3.5	3.9	3.6	3.3	3.5	3.9	3.4
# sacs implanted	495	162	45	7	369	107	40	14
Implantation rate	19.3%	13.0%	8.4%	3.2%	20.8%	13.1%	10.3%	9.0%

Conclusions

This study, though retrospective, convincingly demonstrates – based on the large number of cases – that ICSI does not adversely affect the chance of a frozen embryo from implanting.

The smallest group was the one ≥ age 43: 61 frozen ETs with ICSI vs 46 with conventional insemination. Confounding variables could account for the trend for higher pregnancy and implantation rates. However it may be that the older egg is less likely to withstand the rigors of freeze-thawing when it has been previously punctured with ICSI. Of course this is the group that makes fewer eggs and probably has the least extra embryos to freeze.

References

- [1] Palermo G., Joris H., Derde M.-P., Camus M., Devroey P., Van Steirteghem A.C.: "Sperm characteristics and outcome of human assisted fertilization by subzonal insemination and intracytoplasmic sperm injection". *Fertil. Steril.*, 1993, 59, 826.
- [2] Van Steirteghem A.C., Van der Elst J., Van den Abbeel E., Joris H., Camus M., Devroey P.: "Cryopreservation of supernumerary multicellular human embryos obtained after intracytoplasmic sperm injection". *Fertil. Steril.*, 1994, 62, 775.
- [3] Al-Hasani S., Ludwig M., Gagsteiger F., Kupker W., Sturm R., Yilmaz A. *et al.*: "Comparison of cryopreservation of supernumerary pronuclear human oocytes obtained after intracytoplasmic sperm injection (ICSI) and after conventional in-vitro fertilization". *Hum. Reprod.*, 1996, 11, 604.
- [4] 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.
- [5] 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*, 1997, 2 (CD-ROM).
- [6] Check J.H., Brittingham D., Swenson K., Wilson C., Lurie D.: "Transfer of refrozen twice-thawed embryos do not decrease the implantation rate". *Clin. Exp. Obstet. Gynecol.*, 2001, 28, 14.
- [7] Check J.H., Swenson K., Summers-Chase D., Choe J.K., Yuan W.: "Effect of transferring frozen-thawed embryos resulting from fertilization of immature oocytes matured one day in culture prior to intracytoplasmic sperm injection (ICSI) on implantation rates". *Clin. Exp. Obstet. Gynecol.*, 2003, 30, 197.

Address reprint requests to:
J.H. CHECK, M.D., Ph.D.
7447 Old York Road
Melrose Park, PA 19027 (USA)