

Fertilization by intracytoplasmic sperm injection with sperm with subnormal morphology using strict criteria results in lower live delivered pregnancy rates following frozen embryo transfer rather than eggs fertilized conventionally

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Summary

Purpose: To determine if fertilization by intracytoplasmic sperm injection (ICSI) lowers pregnancy rates following frozen embryo transfer compared to conventional insemination similar to findings with fresh embryo transfer. **Methods:** Clinical and live delivered pregnancy and implantation rates were compared according to whether the eggs were fertilized by conventional oocyte insemination vs ICSI over a 10-year period in women whose husbands had normal semen parameters except for having normal strict morphology between 2-5%. **Results:** The clinical and live delivered pregnancy rates were 40.9% and 31.9%, respectively, with ICSI vs 44.2% and 38.3% for women having conventional insemination. The difference in live delivered pregnancy rates approached statistical significance. **Conclusions:** Choosing ICSI for subnormal morphology may not only possibly lower the chance of successful pregnancy following fresh embryo transfer but possibly also following frozen embryo transfer.

Key words: Intracytoplasmic sperm injection; Frozen embryo transfer; Live delivered pregnancy rate; Strict morphology; Sperm.

Introduction

Initially Van Steirteghem *et al.* suggested that fertilization with ICSI produced extremely low pregnancy rates following the transfer of frozen-thawed oocytes [1]. However, other data was not in agreement finding similar pregnancy rates following frozen ET despite fertilization with ICSI versus fresh embryo transfer pregnancy rates after fertilization by ICSI [2].

Recently some data, especially in younger women, suggested that fertilization by ICSI compared to conventional oocyte insemination resulted in lower pregnancy rates following embryo transfer [3].

To support or refute the conclusion that ICSI may lower implantation rates the present study evaluated pregnancy rates following frozen embryo transfer in couples with oocytes fertilized by ICSI vs conventional oocyte insemination.

Materials and Methods

A retrospective review of frozen ETs over a 10-year time period was performed. There was a requirement of ≥ 2 embryos transferred in women aged ≤ 36 to be included in the study.

Clinical and delivered pregnancy rates were determined according to whether ICSI or conventional oocyte insemina-

tion was performed. The only couples selected were those where all semen parameters were normal except for strict morphology 2-5%.

The option of ICSI or conventional insemination was left up to the couple. The couples were advised that the majority of IVF centers would do ICSI for low normal morphology. They were advised however, that our data does not agree with the importance of poor morphology being associated with decreased fertility [4-6]. They were reminded that by not doing ICSI they would save money, i.e., the cost of ICSI.

The frozen thawed embryos transferred could have been derived from the intentional cryopreservation for risk of ovarian hyperstimulation syndrome or inadequate endometrial thickness, or were supernumerary ones left over in women who previously had fresh embryo transfers.

The cryopreservation method used a simplified slow-cool method avoiding a planar programmable freezer with a one-step removal of the cryoprotectant 1,2 propanediol [7]. Assisted embryo hatching was performed prior to the transfer on day 3 [5].

The clinical (ultrasound evidence of pregnancy at 8 weeks), viable (live fetus at 12 weeks) and live delivered pregnancy rates and implantation rates were then determined according to the method of fertilization.

Results

There were 1,741 frozen embryo transfers evaluated of which 1,039 (59.6%) had ICSI performed and 702 (40.4%) had conventional oocyte insemination.

The clinical pregnancy rate per transfer was 40.9% for ICSI and for conventional insemination it was 44.2%

Revised manuscript accepted for publication December 1, 2008

($p = 0.119$) with chi-square analysis. The live delivered pregnancy rate per transfer was 31.9% for ICSI and for conventional oocyte insemination it was 38.3% ($p = 0.063$) with chi-square analysis.

The clinical pregnancy rates, miscarriage rates and implantations rates are shown in Table 1.

Table 1. — Pregnancy rates for conventional and ICSI insemination following transfer of frozen-thawed embryos.

	ICSI	Conventional
# transfers ≥ 2 embryos transferred	1039	702
# pregnancies including chemical	497	359
% pregnant/transfers	47.8	51.1
# clinical pregnancies	425	310
% clinical/transfers	40.9	44.2
# chemical pregnancies only	70	41
# ectopic	2	8
# viable	359	283
% viable/transfers	34.6	40.3
# miscarriages	94	41
% miscarriage/clinical pregnancy	22.1	13.2
# deliveries	331	269
% delivered	31.9	38.3
# embryos transferred	3142	2219
Average # embryos transferred	3.0	3.2
# sacs implanted	627	463
Implantation rate	20.0%	20.9%

Discussion

The results with frozen ET do not show as great of a difference in pregnancy rates following frozen embryo transfer according to whether fertilization had been performed by ICSI or conventional oocyte insemination as was shown with fresh embryo transfer when comparing these two types of oocyte fertilization procedures [3]. Nevertheless, there was a trend for a higher live delivered pregnancy rate, almost approaching a statistically significant difference, in favor of conventional insemination. There was a 20% higher live delivered rate by not performing ICSI.

Previously, it was found that for women with normal day 3 serum FSH undergoing IVF with normal morphology at 2-5% by strict criteria the failed fertilization rate was 1.3% with ICSI vs 1.8% with conventional oocyte insemination [3]. These data thus help support conclusions that were made with fresh embryo transfer, that if semen parameters are otherwise normal but strict normal morphology is between 2-5%, it is definitely more cost effective to fertilize the eggs with a conventional insemination technique rather than ICSI.

These data support the conclusion that either the mechanics of ICSI may cause some subtle damage that

lowers implantation potential despite creating normal appearing embryos, or that there are other more important criteria for selecting "normal" sperm than morphology that is more efficiently achieved by the zona pellucida. Perhaps there are some chemical signals that allow the zona pellucida to select better sperm so that an embryo with greater implantation potential is formed.

Even if one interprets the data that there was no significant difference in the outcomes, the data at a minimum suggest no benefit in performing the more labor intensive and more costly ICSI procedure [3, 9].

Indirectly these data support conclusions that having a low percentage of sperm with normal morphology using strict criteria may not be a very good prognosticator of male subfertility [7-9].

References

- [1] 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.
- [2] Hoover L., Baker A., Check J.H., Lurie D., Summers D.: "Clinical outcome of cryopreserved human pronuclear stage embryos resulting from intracytoplasmic sperm injection". *Fertil. Steril.*, 1997, 67, 621.
- [3] Check J.H., Bollendorf A., Wilson C., Summers-Chase D., Horwath D., Yuan W.: "A retrospective comparison of pregnancy outcome following conventional oocyte insemination vs. intracytoplasmic sperm injection for isolated abnormalities in sperm morphology using strict criteria". *J. Androl.*, 2007, 28, 607.
- [4] Check J.H., Adelson H.G., Schubert B.R., Bollendorf A.: "Evaluation of sperm morphology using Kruger's strict criteria". *Arch. Androl.*, 1992, 28, 15.
- [5] Check M.L., Bollendorf A., Check J.H., Katsoff D.: "Reevaluation of the clinical importance of evaluating sperm morphology using strict criteria". *Arch. Androl.*, 2002, 48, 1.
- [6] Kiefer D., Check J.H., Katsoff D.: "The value of motile density, strict morphology, and the hypoosmotic swelling test in in vitro fertilization-embryo transfer". *Arch. Androl.*, 1996, 37, 57.
- [7] 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.
- [8] 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.
- [9] Keegan B.R., Barton S., Sanchez X., Berkeley A., Krey L.C., Grifo J.: "Isolated teratozoospermia does not affect in vitro fertilization outcome and is not an indication for intracytoplasmic sperm injection". *Fertil. Steril.*, 2007, 88, 1583.

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