

Effect of method of oocyte fertilization on fertilization, pregnancy and implantation rates in women with unexplained infertility

J.H. Check, W. Yuan, M.C. Garberi-Levito, K. Swenson, K. McMonagle

*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 intracytoplasmic sperm injection (ICSI) offers an advantage over conventional oocyte insemination for women undergoing in vitro fertilization (IVF) and embryo transfer for unexplained infertility. **Methods:** A retrospective seven-year review of outcome following IVF with conventional insemination vs ICSI for the category of unexplained infertility. The decision on which method of insemination to use was made by the couple after hearing pros and cons with the consulting physician. **Results:** There was no difference in failed fertilization rates. However, the live delivered pregnancy rates were significantly higher for the group using conventional oocyte fertilization methods. **Conclusions:** Because of increased embryologist time and therefore increased expense to the patient it makes more sense to first try conventional oocyte insemination over ICSI for unexplained infertility, especially since the former results in a significantly higher live delivery rate

Key words: Intracytoplasmic sperm injection; Conventional oocyte insemination; Unexplained infertility.

Introduction

In vitro fertilization-embryo transfer (IVF-ET) revolutionized the treatment of infertility related to mechanical problems with the fallopian tubes. In vitro fertilization-embryo transfer also became a useful treatment for male factor problems. The advent of the process of intracytoplasmic sperm injection (ICSI) even further widened the scope of sperm issues that could be corrected including non-obstructive and obstructive azoospermia and anti-sperm antibodies [1].

IVF-ET has proved very useful for the infertility category of unexplained or cryptic infertility [2]. Theoretically when certain factors have been established: fallopian tube patency, the absence of adhesions, the absence or laser vaporation of endometriosis, the demonstration of follicular maturation, oocyte release, and normal luteal function or adequate exposure to luteal phase progesterone support, normal semen parameters and normal post-coital tests – the persistence of infertility could be related to a tubal motility defect or to a problem with sperm oocyte interaction [2].

In the above infertility scenario extracting the oocytes and incubating them with sperm would obviate the infertility defect. However, there is the possibility that the occult infertility factor is related to the failure of sperm to bind to the zona pellucida or the failure of the sperm to initiate the first phase of oocyte activation. In these circumstances conventional oocyte insemination would fail but ICSI would obviate the problem.

Thus many clinicians advise a couple to fertilize the

oocytes by ICSI rather than conventional insemination when IVF-ET is suggested for unexplained infertility because of a fear of failed or very poor fertilization. Recently however a study comparing outcome following IVF-ET with conventional oocyte insemination vs ICSI for teratozoospermia found a statistically higher (but not clinically important) fertilization rate with ICSI but also found a significantly higher (and clinically important) pregnancy rate with conventional oocyte insemination [3].

The present study retrospectively compared fertilization rates and pregnancy rates in couples with a diagnosis of unexplained infertility undergoing IVF-ET according to whether conventional oocyte insemination vs ICSI was used.

Materials and Methods

A retrospective study during a 7-year time period evaluated fertilization and implantation rates and clinical and live delivered pregnancy rates following IVF-ET in couples whose IVF was being performed for unexplained infertility.

The couples with unexplained infertility of a minimum of one year duration were included if the male partner's evaluation determined a normal semen analysis (including concentration of sperm $\geq 20 \times 10^6/\text{ml}$, % motility $\geq 40\%$, normal morphology using strict criteria $> 4\%$, hypo-osmotic swelling test $> 50\%$, and antisperm antibodies $< 20\%$ using a direct immunobead assay. Furthermore it was required that the female partner demonstrated bilateral patent fallopian tubes by hysterosalpingogram or laparoscopy, a normal post-coital test with intercourse 8-24 hours before, and normal ovulation. The latter consisted of attaining a mature follicle of 18-24 mm by transvaginal sonography associated with a serum estradiol $> 200 \text{ pg/ml}$, release of the egg from the follicle by ultrasound, and normal length of the luteal phase with a mid-luteal phase serum proges-

Revised manuscript accepted for publication June 22, 2010

Table 1. — Fertilization, pregnancy, and implantation rates following conventional oocyte insemination vs intracytoplasmic sperm injection for unexplained infertility.

	Total	Unexplained with ICSI				Total	Unexplained without ICSI			
		≤ 35	Ages 36-39	40-42	≥ 43		≤ 35	Ages 36-39	40-42	≥ 43
# oocytes retrieved	145	77	64	13	5	134	64	56	13	1
# transfers	107	52	43	8	4	91	45	40	6	0
# metaphase II eggs retrieved	1408	811	466	93	38	1552	839	569	143	1
# metaphase II eggs inseminated	1524	879	513	93	39	1693	935	609	148	1
# fertilized	1123	670	361	69	23	1078	606	373	99	0
% fertilized	73.7	76.2	70.4	74.2	59.0	63.7	64.8	61.2	66.9	0.0
# embryos transferred	343	148	141	33	21	293	127	142	24	0
# implanted	61	35	22	2	2	73	38	27	8	0
% implanted/transfer	17.8	23.6	15.6	6.1	9.5	24.9	29.9	19.0	33.3	0
# clinical pregnancies	36	18	14	2	2	48	26	17	5	0
# live delivered	31	18	10	2	1	42	23	14	5	0
% viable/transfer	29.0	34.6	23.3	25.0	25.0	46.2	51.1	35.0	83.3	0
# with failed fertilization	6	2	1	2	1	5	3	1	0	1
% with failed fertilization	4.1					3.7				

terone level > 12 pg/ml. Couples were also included if some of these aforementioned infertility factors were present initially but the couple still failed to conceive after at least six corrected cycles of treatment.

The decision on whether to do conventional oocyte insemination vs ICSI was determined by the couple after consultation with one of four consulting physicians. The couples were explained the main benefits of ICSI: the possibility that the unexplained infertility was related to failure of zona pellucida binding or the first step of oocyte activation which would continue to fail with conventional oocyte insemination but probably succeed with ICSI [4].

The couples were explained the potential benefit of conventional oocyte insemination: less expense and gaining the knowledge as to whether IVF-ET was their only option, i.e., if conventional oocyte insemination resulted in failed or very poor fertilization but subsequent ICSI produced good quality embryos, the couple would know that IVF-ET and ICSI was their only recourse to have a baby with their own gametes. Otherwise they could choose to return to less expensive treatment options hoping previous failures were related to bad luck.

Some couples were also advised of the data suggesting that the transfer of embryos derived from oocytes fertilized by ICSI when using sperm with poor morphology resulted in lower pregnancy rates in one study [3]. The reason why only some but not all the couples were advised of this study was related to the fact that despite all four physicians were part of one reproductive endocrine/infertility group not all physicians were aware of these data.

Physicians involved in oocyte retrieval and embryo transfer are assigned these duties on a weekly basis and thus the physician performing the oocyte retrieval frequently had nothing to do with the decision on the method of insemination. In vitro fertilization cycles in which half of the oocytes were fertilized by conventional technique and half with ICSI were not included in the study.

Results

There was a significantly higher fertilization rate with ICSI (73.7%) vs conventional oocyte insemination (63.7%) ($p < 0.001$, chi-square analysis) as seen in Table 1.

There was a significantly higher clinical pregnancy rate with conventional oocyte insemination (52.7%) vs ICSI (33.6%) ($p = 0.0012$) as seen in Table 1. There was also a significantly higher live delivered pregnancy rate with conventional (46.2%) vs ICSI (29.0%) ($p = 0.0165$) (Table 1).

Moreover there was a significantly higher implantation rate with conventional (24.9%) vs ICSI (17.8%) ($p = 0.036$) while the failed fertilization rate was similar with ICSI (4.1%) and conventional oocyte insemination (3.7%) (Table 1).

Conclusions

The statistically higher fertilization rate found with ICSI is not nearly as clinically important as the statistically higher clinical and live delivered pregnancy rate with conventional insemination.

The risk of failed fertilization was not higher with conventional oocyte insemination and thus should not be considered a reason for choosing ICSI for unexplained infertility. Failure of sperm to attach to the zona pellucida or initiate the first phase of oocyte activation does not seem to be a frequent etiologic factor for unexplained infertility.

IVF-EF seems to provide an adequate chance of achieving a successful pregnancy for the category of unexplained infertility. Based on similar risks of failed fertilization, increased expense, increased embryologist time, and lower pregnancy rates it makes more sense to attempt conventional oocyte insemination for IVF rather than ICSI when faced with unexplained infertility. Based on these data, strategies of splitting the group of oocytes and using both methods of fertilization do not seem to offer any advantages.

Acknowledgment

We would like to thank Ascend Specialty Rx for providing partial grant support.

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] Check J.H.: "Cryptic infertility and therapeutic options". *Clin. Exp. Obstet. Gynecol.*, 2001, 28, 205.
- [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., Summers-Chase D., Cohen R., Brasile D.: "Artificial oocyte activation with calcium ionophore allows fertilization and pregnancy in a couple with long term unexplained infertility where the female partner presently has diminished egg reserve and failure to fertilize oocytes despite intracytoplasmic sperm injection". *Clin. Exp. Obstet. Gynecol.*, 2010, 37, 263.

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