

# Pregnancy rates per embryo transfer (ET) may be improved by conventional oocyte insemination for male factor rather than intracytoplasmic sperm injection (ICSI)

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## Summary

**Purpose:** To determine if intracytoplasmic sperm injection (ICSI) for mild male factor may create embryos less likely to implant. **Method:** A retrospective analysis of pregnancy outcome following oocyte fertilization with ICSI vs conventional egg insemination was performed. **Results:** Though there were many less cases using conventional oocyte insemination compared to ICSI so that a meaningful comparison of outcome could not be made, the data could suggest the fertilization by ICSI might result in embryos less likely to implant. **Conclusions:** This pilot study should encourage IVF centers to consider conventional oocyte insemination for mild male factor instead of ICSI. Only by evaluating a larger series can it be determined with certainty that fertilization by ICSI may lower the implantation potential of the embryo that is formed.

**Key words:** Intracytoplasmic sperm injection; Conventional oocyte insemination; Embryo implantation.

## Introduction

The introduction of intracytoplasmic sperm injection (ICSI) has allowed successful conception by males with sperm of such poor quality that it would not have been likely with either intrauterine insemination (IUI) or conventional insemination of oocytes as part of in vitro fertilization (IVF) that a pregnancy would have been achieved [1, 2].

In vitro fertilization is expensive and labor intensive for both patient and physician. Thus many IVF centers (including our own) fearing failed fertilization may suggest ICSI to "play it safe" for milder male factor cases that in the past usually resulted in fertilization.

The possibility exists that the zona pellucida may be better able to select the best sperm to result in the best embryo as opposed to the embryologist selecting the best morphologic sperm. The present study probed the question as to whether performing ICSI for mild to moderate male factor problems may have a detrimental effect on pregnancy rates.

## Materials and Methods

A retrospective review over a three-year period was performed in all IVF cycles whether ICSI or conventional insemination was used where the diagnosis included male factor. The general policy at the Cooper Center for IVF is to recommend ICSI for male factor for the reasons stated in the introduction. The general reason for a woman not choosing ICSI is to save money with conventional insemination.

The definition of male factor included: motile density < 8 x 10<sup>6</sup>/ml, motility < 30%, sperm morphology using standard WHO criteria or with strict criteria  $\leq$  4% normal, the presence of anti-sperm antibodies  $\geq$  80% using direct immunobead assay, and a hypo-osmotic swelling test (HOST) score < 50%. Cases involving testicular and epididymal sperm aspiration were excluded.

Pregnancy outcome was then determined and compared for each group – ICSI vs conventional insemination. The data was also stratified according to two age groups: < 35 and 36-39.

Only cycles with at least two embryos transferred were evaluated. A clinical pregnancy was one where there was ultrasound evidence of pregnancy. A delivered pregnancy was one where a live baby was born.

## Results

Pregnancy outcome according to method of oocyte insemination is shown in Table 1. As predicted only 29 of the 541 transfers (5.3%) were with conventional insemination. There were 118 ICSI cycles performed for low HOST or positive antisperm antibodies and all used ICSI.

There were 51 clinical pregnancies (43.2%) and 48 live delivered pregnancies (40.6%) for this subgroup of low HOST scores and positive antisperm antibodies. Failed fertilization occurred in two of 31 retrievals (6.4%) using conventional insemination and in five of 517 (0.96%) using ICSI ( $p = \text{NS}$ ).

There were 329 transfers in women aged  $\leq$  35 and 183 in women aged 36-39 where ICSI was used. Clinical pregnancies occurred in 159 and 69 women, respectively (48.3% and 37.7%). The delivered pregnancy rates were 145/329 (44.1%) for women  $\leq$  35 and 58/183 (31.7%) for women 36-39.

For women having conventional oocyte insemination 16/21 (76.2%) aged  $\leq$  35 achieved a clinical pregnancy while 5/8 (62.5%) women aged 36-39 achieved one. The

live delivered pregnancy rates were 66.7% (14/21) and 62.5% (5/8), respectively.

Overall for women  $\leq 39$  there were 253 clinical pregnancies in 512 transfers (49.4%) for oocytes fertilized with ICSI vs 21/29 (72.4%) with conventional insemination ( $p < 0.05$ , chi-square analysis). There were 224/512 (43.7%) delivered pregnancies for women  $\leq 39$  with ICSI vs 19/29 (65.5%) for conventional insemination ( $p < 0.05$ , chi-square analysis). The implantation rate was also significantly higher with conventional insemination vs ICSI ( $p < 0.01$ , chi-square analysis) (Table 1).

Table 1. — Pregnancy outcome following embryo transfer according to method of oocyte fertilization.

	Male factor with ICSI			Male factor without ICSI		
	Total	$\leq 35$	36-39	Total	$\leq 35$	36-39
# transfers	512	329	183	29	21	8
% mature eggs retrieved	75.9	75.4	76.1	85.2	84.4	93.3
% mature eggs fertilized	64.5	64.6	66.4	62.7	61.5	70.1
Average # ET	3.2	3.0	3.3	3.2	3.1	3.4
% clinical pregnancy/transfer	44.5	48.3	37.7	72.4	76.2	62.5
% delivered pregnancy/transfer	39.6	44.1	31.7	65.5	66.7	62.5
# embryos transferred	1831	991	607	107	65	27
# embryos implanted	376	246	101	35	25	10
% implanted	20.5	24.8	16.6	32.7	38.5	37.0

## Discussion

In our own experience the cut-off values for normal motile density or standard or strict morphology have not been very effective in predicting subfertile males either following intercourse, intrauterine insemination, or IVF with conventional insemination [3-7]. The long distance from cervical os to fallopian tube certainly favors the natural state of the sperm with the best motility.

The theoretical advantage of performing IVF with ICSI is the ability to ensure fertilization by one of the best morphologic sperms. However, one study comparing the effects of single sperm defects on pregnancy outcome following conventional oocyte insemination found a clinical pregnancy rate almost twice as high with sperm with strict morphology of  $\leq 4\%$  as compared to sperm which were considered without any abnormalities in motile density or morphology [7].

Thus, these new data are consistent with the hypothesis that certain properties of the zona pellucida allow the selection of sperm that have a better chance of resulting in a live pregnancy than selection of sperm with the best morphology by the andrologist/embryologist.

Though the results do show a significant difference between ICSI and conventional insemination in both clinical and ongoing/delivered pregnancy rates one should always use caution when interpreting a retrospective study especially when the sizes of the two study groups are so disproportional and one group very small in comparison.

It is hoped that this study will generate interest in other IVF centers to retrospectively evaluate their data in a similar manner and see if the same conclusions are reached. More importantly the present study may stimu-

late interest in a multicenter prospective cooperative study to better test this hypothesis.

The small numbers in the group having conventional oocyte insemination were too low to show a significant difference in failed fertilization with conventional insemination vs ICSI (6% vs 1%). However, if a large multicenter prospective study found the same results then one would have to determine if the improved pregnancy outcome with conventional oocyte insemination offsets the risk of failed fertilization.

Confirmation of this data could lead to a change in treatment philosophy, such as for alleged mild male factor, to inseminate at least half of the oocytes conventionally but do some percentage with ICSI as a back-up for failed fertilization. If the embryos formed have equal morphologic characteristics then the ones from conventional insemination should be transferred first, and the ones formed by ICSI frozen. Despite some initial data suggesting that embryos formed by ICSI do not freeze as well, subsequent studies found that not be the case [8-10].

These data will encourage our group to try more cases with mild male factor to attempt fertilization through conventional methods rather than ICSI allowing us to evaluate a larger series in the future.

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