

## Should We Do Routine or Selective ICSI?

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Intracytoplasmic sperm injection (ICSI) was originally designed to treat those with male factor infertility or with non male factor infertility after failure of the conventional IVF. However due to the good results obtained with ICSI many centers nowadays prefer to use routine ICSI.

Before we can agree with this opinion we have to answer two main questions. The first one is the superiority of ICSI results over the conventional IVF results and the second is drawbacks of ICSI.<sup>1</sup>

### **The superiority of ICSI results over the conventional IVF results. Is it true the ICSI has better results than conventional IVF?**

The success rate in ICSI is generally higher than the success rate in IVF when used for treatment of male factor infertility. This has been explained by the following:<sup>2</sup>

1. Women treated with ICSI usually present at a younger age compared to those treated for IVF who usually have had many years of treatment for their tubal problems (e.g. tubal surgery, laparoscopic surgery, etc.)
2. Women treated with ICSI have a healthy pelvis with no previous infections or adhesions. It is worth recalling here the fact that women with hydrosalpinges or endometriosis have a lower success rates with IVF, probably due to the abnormal humoral environment of their pelvises.<sup>3</sup>
3. Performing ICSI necessitates drilling a hole in the zona pellucida by the injection pipette. This hole may make it easier for the blastocyst to hatch and attach to the uterine wall, a form of assisted hatching (vide infra).

The higher success rate in ICSI compared to IVF has lead many groups to suggest performing ICSI in all cases of tubal infertility (rather than IVF). However, the results of ICSI were not better than IVF in those patients confirming the fact that a healthy pelvis plays an important factor in the better results seen in ICSI.<sup>2</sup>

Comparing between Pregnancy rates per treatment cycle with ICSI & the incidence of pregnancy loss (i.e. subclinical pregnancies, clinical abortions and ectopic pregnancies), The results suggest that the overall obstetric outcomes of these pregnancies are similar those obtained after conventional IVF.<sup>4</sup>

A recent Cochrane Systemic Review included eight randomized control trials compared ICSI with conventional IVF and showed that for couples with normal semen fluid analysis there was no difference in fertilization rates or pregnancy rates for the different groups.<sup>5</sup>

### **The drawbacks of ICSI. Does ICSI increase the incidence of congenital fetal malformations?**

A significant number of men with infertility, particularly those with azoospermia or severe oligozoospermia, have a genetic etiology for reproductive failure.<sup>6</sup> The broad categories of identified genetic associations with male infertility include several disorders.

The concerns that genetic factors associated with male infertility may be transmitted to the next generation have been magnified by emerging anxieties that the ICSI technique itself may result in an increased risk of genetic abnormalities in potential offspring. Thus, although the use of ICSI for couples with severe male-factor infertility has greatly increased the prospects of parenthood for many men, it behoves us to evaluate critically the safety issues implicit in the technology, particularly with respect to the health of children born as a result.<sup>6</sup>

### **The biological basis for genetic concerns with ICSI**

#### **ICSI using mature sperm:**

ICSI represents one of the most important advances in the treatment of the subfertile male; however significant concerns exist regarding possible harmful effects of its use.

Principal concerns relate to the potential for transmission of abnormal genes to offspring.<sup>6</sup>

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This may be due to:

1. The bypassing of the selection mechanisms against pathologically or genetically abnormal spermatozoa.
2. The fertilization of abnormal oocytes (during natural fertilization or IVF a natural selection process is accepted to be in action). Therefore it is less likely for abnormal oocytes to fertilize successfully during these processes, often due to the inability of sperm to penetrate. However, during ICSI this process of selection by sperm penetration is bypassed. The only selection criterion used for ICSI is the normal look of the oocyte, which is a highly subjective process.
3. The altered environment or mechanical and chemical damage to the oocyte, which might in turn lead to perturbations of meiosis and mitosis.
4. Various chemical or environmental toxins, which might lead to point mutations, resulting in genetic diseases visible at birth.

#### ICSI using immature sperm:

With immature sperm, nuclear maturation processes may be incomplete, and some studies have suggested that spermatid chromatin may be more unstable and more vulnerable to denaturing stress than the chromatin of mature spermatozoa.

Certain genetic syndromes are linked to disturbances in genomic imprinting and, although preliminary results have so far failed to show abnormalities in the limited numbers of offspring derived from such techniques, caution is advised.<sup>6</sup>

#### Evidence of genetic abnormality in offspring

The occasional increase in de novo chromosomal aberrations encountered is probably linked directly to the characteristics of the infertile men treated rather than to the ICSI procedure itself.<sup>7</sup>

There are conflicting reports regarding the mental development of children born following ICSI.<sup>8</sup> Although so far, ICSI children did not prove to have any slower mental development than the general population, it is suggested that further studies controlling for parental background and other confounding variables, are needed before conclusions can be drawn.

So, prior to commencing treatment, couples should be informed of the available data relevant to the risk of transmitting chromosomal aberrations, the risk of de novo, mainly sex

chromosomal aberrations and the risk of transmitting fertility problems to the offspring.

Couples should also be reassured that so far, there seems to be no higher incidence of congenital malformations in children born after ICSI.

Keeping in mind the higher success rate of ICSI when compared to the conventional IVF when used for treatment of male factor infertility versus the potential harmful effects of its use, ICSI should be the procedure of choice for those cases of male infertility or after failure of the conventional IVF in cases of tubal infertility and cases of unexplained infertility. The routine use of ICSI in all cases requiring IVF is still a matter of scientific debate.

#### References

1. Palermo G, Joris H, Devroey P, et al. Pregnancies after intracytoplasmic injection of single spermatozoon into an oocyte. *Lancet*. 1992; **340**: 17.
2. Aboulghar M, Mansour R, Serour G, et al. Prospective controlled randomized study of in vitro fertilization versus intracytoplasmic sperm injection in the treatment of tubal factor infertility with normal semen parameters. *Fertil Steril*. 1996; **66**: 753.
3. Camus E, Poncelet C, Goffinet F, et al. Pregnancy rates after in-vitro fertilization in cases of tubal infertility with and without hydrosalpinx: a meta-analysis of published comparative studies. *Hum Reprod*. 1999; **14**: 1243.
4. Wisanto A, Magnus M, Bonduelle M, et al. Obstetric outcome of 424 pregnancies after intracytoplasmic sperm injection (ICSI). *Hum Reprod*. 1995; **10**: 2713-8.
5. Van Rumste M, Evers J, Farquhar C, et al. Intracytoplasmic sperm injection versus partial zona dissection, subzonal insemination and conventional techniques for oocyte insemination during invitro fertilization (Cochrane Review). The Cochrane Library. 1999.
6. Bonduelle M, Willikens J, Buysse A, et al. Prospective study of 877 children born after intracytoplasmic sperm injection, with ejaculated, epididymal and testicular spermatozoa and after replacement of cryopreserved embryos obtained after ICSI. *Hum Reprod*. 1996; **11** Suppl **4**: 131-59.
7. Bonduelle M, Camus M, DeVos A, et al. Seven years of intracytoplasmic sperm injection and follow-up of 1987 subsequent children. *Hum Reprod*. 1999; **14** Suppl **1**: 243-64.
8. Bowen J, Gibson F, Leslie G, et al. Medical and developmental outcome at 1 year for children conceived by intracytoplasmic sperm injection. *Lancet*. 1998; **351**: 1529-34.

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