Intra-Cytoplasmic Sperm Injection (ICSI)

HUMAN FERTILISATION & EMBRYOLOGY AUTHORITY

Introduction

The Human Fertilisation and Embryology Authority (HFEA) is the statutory body that regulates *in vitro* fertilisation (IVF) treatments including ICSI. One of the HFEA's responsibilities is to give advice and information to people seeking licensed fertility treatment. The HFEA has produced this leaflet to explain some of the recent medical and scientific studies relating to the use of ICSI and the implications this may have for patients.

Before deciding upon a particular treatment, patients should have an opportunity to weigh up the benefits and risks of that treatment. Your treatment centre is required by law to offer you counselling about the implications of any proposed treatment. It is important that the counselling offered to you should include genetic implications, especially for men who have very few sperm (severe oligozoospermia) or no sperm (azoospermia) in their semen, and men with Klinefelter's Syndrome. Pre-natal diagnosis may be of help in considering individual risks. The centre will also be able to provide you with information specifically about ICSI, and answer any questions you may have. This leaflet deals with general issues surrounding the ICSI technique.

ICSI was introduced into clinical treatment for certain types of infertility in 1992. ICSI is a type of IVF treatment that involves the injection of a single sperm straight into each egg. The fertilised egg (embryo) can then be transferred into the womb of the woman as in a normal IVF cycle. ICSI is a relatively new technique but has already helped many couples.

The live birth rates for ICSI and conventional IVF are similar (about 23% per cycle in the most recently published HFEA data).

What does ICSI involve?

ICSI is similar to conventional IVF in that gametes (eggs and sperm) are collected from each partner. To achieve fertilisation, a single sperm is taken up in a fine glass needle and is injected directly into an egg. The eggs are then incubated and examined. Usually one or two embryos may then be transferred back into the womb of the woman two or three days after fertilisation. Some eggs may not survive the injection process and not all eggs collected will be of a high enough quality or mature enough to be suitable for injection.

When is ICSI used?

In conventional IVF the eggs and the sperm are mixed together in a dish and the sperm fertilise the eggs naturally. ICSI bypasses the natural processes involved in a sperm penetrating an egg, and is therefore used when there are problems that make it difficult to achieve fertilisation naturally or by conventional IVF. Circumstances

in which ICSI may be appropriate include:

- When the sperm count is very low
- When the sperm cannot move properly or are in other ways abnormal
- When sperm has been retrieved directly from the epididymis (PESA) or the testicles (TESA/TESE), from the urine, or by electroejaculation
- When there are high levels of antibodies in the semen
- When there have been previous fertilisation failures

Patients who do not fall into these categories may wish to discuss any concerns about their treatment with their clinician.

Men who have very few sperm (oligozoospermia) or no sperm (azoospermia) in their semen, or who have high numbers of abnormal sperm that are unable to fertilise an egg, would previously have had little or no chance of fathering their own genetic offspring. ICSI offers these men and their partners real hope of having a genetically related child.

What are the risks of ICSI treatment?

ICSI like IVF is an invasive procedure. However, unlike IVF, ICSI involves injecting a sperm directly into an egg, therefore allowing the use of sperm that may not otherwise be able to fertilise an egg. For these reasons, concerns about the potential risks to children born as a result of ICSI have been raised, and several follow-up studies have been published.

The HFEA reviews the evidence on an ongoing basis. ICSI is still a relatively new technique, and all children conceived using ICSI are still very young. Consequently, these follow-up studies involve relatively small numbers of children and do not include effects that may only be seen in older children or in the next generation. The HFEA considers follow-up studies to be extremely important and would encourage patients to talk to their treatment centre about participation in such studies.

Clearly, more studies are needed, but the use of ICSI has been potentially linked with certain genetic and developmental defects.

- Possible inheritance of genetic and chromosomal abnormalities:

  Inheritance of cystic fibrosis gene mutations.

  Some men who have no sperm in their semen are found to have congenital bilateral absence of the vas deferens (CBAVD). In this condition, the tubes that carry sperm from the testes to the penis are missing. Two thirds of men with CBAVD are also carriers of certain cystic fibrosis mutations. Men with CBAVD and their partners may therefore wish to undergo genetic testing before proceeding with ICSI. Your treatment centre should be able to give you more information and counselling about the implications of genetic testing.

  Sex chromosome defects and the inheritance of sub-fertility.

  A small proportion of sub-fertile men have parts of the Y chromosome missing (deleted). Certain genes on the Y chromosome have been shown to be involved in the production of sperm, and deletion of these genes may be responsible for some men having few or no sperm in their semen. Consequently, using sperm with such deletions to create an embryo may result in the same type of sub-fertility being passed from father to son.

  Abnormal numbers or structures of chromosomes, particularly the sex chromosomes (X and Y), may be associated with infertility in both men and women, and babies born from ICSI treatment may have a slightly increased risk of inheriting these abnormalities. Studies have found that up to 3.3% of fathers of ICSI babies have abnormal chromosomes. It is estimated that up to 2.4% of the wider population have a chromosomal abnormality.

- Novel chromosomal abnormalities:

  The complexity of the process of egg and sperm production means that even if an individual possesses a normal number of chromosomes, their gametes could potentially have an abnormal number. It is not possible to detect beforehand which eggs or sperm have chromosomal abnormalities, and gametes that might not have been able to participate in natural fertilisation could therefore be used in ICSI. Babies born after ICSI have

been reported to have new chromosomal abnormalities in up to 3% of cases. The rate in the general population is around 0.6%.

- Possible developmental and birth defects:

  Birth defects.

  There is not yet any clear evidence whether ICSI results in higher rates of birth defects. The number of babies reported to have major birth defects, such as cleft palate, is between one and five % in both the general population and in babies born following ICSI. Studies suggest that minor abnormalities occur in up to 20% of ICSI babies, compared to up to 15% of the population. For example, one recent study has shown a three fold excess risk in the rate of the relatively rare problem hypospadias following ICSI. More studies are needed in order to gain further insight into these possible effects.

- Possible risks during pregnancy:

  Miscarriage.

  With ICSI, it is possible that abnormal gametes, which would not usually be able to produce a viable embryo, could be used. This may increase the chance of an abnormal embryo being formed. However, most abnormal embryos will not implant into the womb and grow, but some might, leading to a possible higher risk of miscarriage. It has been reported that the risk of miscarriage increases in proportion to the severity of male infertility.

Medical and scientific information changes rapidly and the HFEA endeavours to keep patients and clinicians up to date with all relevant developments to help patients review their treatment options.

Glossary

Azoospermia – *complete absence of sperm in the ejaculate.*

Electroejaculation – *the use of electrical stimulation to aid production of a semen sample in impotent or paralysed men.*

Epididymis – *coiled tubing outside the testicles which store sperm.*

Gametes – *male sperm and female eggs.*

Hypospadias – *congenital abnormality, affecting male offspring, in which the opening of the urethra is misplaced or malformed.*

Klinefelter's Syndrome – *men with an extra X chromosome, thus his chromosome complement is 47XXY.*

Oligozoospermia – *low numbers of sperm in the ejaculate.*

PESA - *Percutaneous Epididymal Sperm Aspiration, involving sperm being retrieved directly from the epididymis using a needle.*

TESA – *Testicular Sperm Aspiration, involving sperm being retrieved directly from the testes using a needle.*

TESE – *Testicular Sperm Extraction, involving sperm being retrieved from a biopsy of testicular tissue.*

Further information

Information and advice about fertility treatment is available from a GP or consultant, the clinicians, nurses and counsellors at a clinic. Each clinic produces its own patient information describing the services available and explaining what is involved in treatment. In addition, information is available from patient organisations such as ISSUE (www.issue.co.uk Tel: 09050 280300) and CHILD (www.child.org.uk Tel: 01424 732361).

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