IVF Treatment by Intracytoplasmic Sperm Injection - ICSI

Patient Information

Summary of IVF Treatment with ICSI

ICSI, where a single sperm is injected directly into the centre of the egg, is offered when there is a concern about the fertilising potential of the sperm.

Who is ICSI suitable for?

ICSI enables men with sperm problems to achieve fertilisation which would otherwise have been unlikely or impossible. It will be recommended in the following scenarios:

- Where previous IVF treatment has resulted in complete failed fertilisation or low fertilisation rates.
- Where a semen analysis has shown low numbers of sperm (oligozoospermia), low numbers of moving sperm (asthenozoospermia), high numbers of abnormally shaped sperm (teratozoospermia) or a combination of these issues.
- Where a semen analysis shows clinically significant levels of antisperm antibody binding such that there is concern the antibodies will interfere with the normal binding of a sperm to an egg.
- Where sperm DNA fragmentation testing results suggest high levels of DNA damage.
- Where sperm has been frozen and post-thaw survival tests show low numbers of moving sperm.
- ICSI is required if sperm is collected surgically, sperm may be retrieved surgically due to:
    - An almost complete failure of sperm production within the testes such that no sperm are found in the ejaculate (azoospermia).
    - A blockage of the narrow tubes which carry the sperm from the testes, for example as a result of disease, injury, genetic condition or vasectomy.
    - Spinal injuries which have damaged the nerves controlling ejaculation.

The ICSI Procedure

The sperm used for ICSI are collected from the man by whichever method is appropriate for his underlying problem, either by normal ejaculation or surgical sperm recovery. The sperm is then prepared for treatment in such a way as to enable the isolation of moving sperm and removal of other non-sperm cells. The eggs are recovered from the woman by the same method as for in-vitro fertilisation after hormone stimulation of her ovaries. In the laboratory under a microscope, the prepared sperm is added to a viscous solution called polyvinylpyrrolidone (PVP). This solution slows the sperm down to enable isolation and immobilisation of a single, morphologically normal live sperm. Using a hollow glass injection needle, which is several times finer than a human hair, the sperm is immobilised by breaking the sperm tail and then picked up. The selected sperm is then injected into the fluid centre (the cytoplasm) of each egg; this carries the sperm through its physical barriers. The sperm now has a chance to fertilise the egg, where otherwise it may have struggled. There is a small risk that the egg may not survive the injection procedure; this occurs for around 5% of eggs.

ICSI results

Whilst the sperm is injected directly into the egg, unfortunately it doesn't guarantee fertilisation as a cascade of events needs to occur. Despite this, even in cases of men with very severe sperm problems, our results with ICSI are highly successful. 95% of patients achieve a single blastocyst embryo transfer and 60% have a further blastocyst embryo(s) stored. Please note where surgically retrieved sperm is used results may be lower. The woman's age is the most important factor that determines the chance of pregnancy and the successful birth of a baby. A summary of our latest results, the pregnancy and birth rates we have achieved during the past few years, are given in a separate information sheet.

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Issues to consider before ICSI treatment

ICSI is a remarkable and successful treatment of male infertility. The first child to be born as a result of ICSI was delivered in 1992 and ICSI has now led to the birth of hundreds of thousands of babies throughout the world. Regarding the safety of ICSI, published evidence so far is largely reassuring. There is a large amount of data on its short-term safety, but it will be some years before there is sufficient information about any long-term effects for children conceived in this way. Regardless of the largely reassuring evidence, ICSI should only be recommended where it is clear that its use would benefit the patient.

Birth defects

There have been several follow up studies carried out worldwide relating to children born as a result of IVF or ICSI treatment. Studies have suggested a link between any type of assisted reproductive technology and an increased risk of birth defects compared to spontaneously conceived children. Further increases have been described when comparing ICSI to IVF. While most studies suggest an increased risk of birth defects, the overall absolute risk is considered to be small, and it is therefore an appropriate treatment to recommend where there are indications that its use would increase the chances of conception. It should be noted that certain birth defects affecting the genital tract of male infants maybe increased due to the fertility problems in general, rather than treatment with ICSI.

Pregnancy outcomes

There is evidence that associates poorer pregnancy outcomes following IVF and ICSI, including lower birthweights and earlier deliveries. These risks are considered to be low and for some this may be due in part to the factors associated with the cause of infertility rather than the treatment itself.

Chromosome abnormalities

There is some evidence that some rare chromosome disorders may be slightly more common in children born as a result of ICSI treatment. These are conditions where an extra sex chromosome (either an X or Y chromosome) is present. For some men with severe male factor infertility the cause of infertility is due to chromosomal disorders, for example microdeletions on the Y chromosome. Where this is the cause, if ICSI is used to ensure conception where otherwise it would not have happened, there is mixed evidence as to whether the chromosomal abnormalities are likely to be passed on. It is therefore possible male offspring may inherit similar infertility issues to their father. For this reason, we strongly advise a chromosome analysis and genetic screening before ICSI treatment in men with a sperm count below 5 million/ml and for men considering surgical sperm recovery because of failure of sperm production within their testes. Even if there is no clear indication for genetic testing of a man before treatment, there is a theoretical possibility of ICSI causing subtle undetectable genetic defects or assisting the passage of existing genetic defects such as those affecting the fertility of male offspring. There is no special need for prenatal genetic testing to be done during pregnancy just because of the ICSI procedure.

Developmental delay

Because ICSI is a relatively new technique we have little information on the long-term development and health of children born after ICSI, however studies performed so far have been reassuring suggesting that the vast majority of children born after ICSI treatment

develop normally. It has recently been suggested that there may be a very small increase in the rates of autism and developmental delay in children born following ICSI treatment, however this increase is likely to be a small one – perhaps an additional one or two cases per 10000 children.

Some studies suggest an association between the incidence of cerebral palsy and IVF or ICSI, however there is conflicting evidence thus far due to other factors that could cause cerebral palsy affecting the analysis. There may therefore not be a true association, or if there is, the level of risk is likely to be very low.

For couples considering surgical sperm recovery for ICSI because the man has a congenital absence of the connecting tubes from his testes (the vas deferens), we advise some specific genetic tests.

Imprinting disorders

Every human has two complete sets of chromosomes, one set originating from the egg provider and one from the sperm provider. A gene is said to be imprinted when one of the two genes is "turned off" via attachment of specific modifiers or changes to how DNA is packaged within a cell. This imprinting is reversable at certain points, including during the time where ovarian stimulation is taking place, blastocyst embryo culture and just after fertilisation. Where modifiers are attached to the DNA, the genetic code (DNA) is itself unmodified; only the resultant gene expression changes which is known as epigenetics. Less than 1% of human genes are imprinted, but the imprinting is important, as where it goes wrong growth and development of the foetus can be affected leading to imprinting disorders such as Prader-Willi syndrome or Angelman syndrome. These disorders can lead to changes in the development, metabolism and growth of a child. Some evidence suggests that any assisted reproductive technology (IVF or ICSI) can cause an increased risk of imprinting disorders due to interference as a result of ovarian stimulation and embryo culture at the point epigenetic changes are occurring. These risks appear to be further increased where ICSI has been used. Despite this, most studies agree that the evidence is equivocal, in that there is not enough evidence to prove the treatment in itself is the cause or that there is a quantifiable increase. Therefore, until further long-term studies are done, any risk, if there is, should be considered low. The possible increased risk associated with ICSI is thought to be explained by the fact that in most cases ICSI is used to overcome male factor infertility. The underlying sperm issues could lead to disruption of epigenetic changes within the sperm, such that the increase associated with ICSI maybe explained.

Surgical sperm recovery for congenital bilateral absence of the vas deference (CBAVD)

For couples considering surgical sperm recovery for ICSI because the man has a congenital absence of the connecting tubes from his testes (the vas deferens), we advise some specific genetic tests. It is well-recognised that the abnormal genes which cause some men to have congenital absence of their vas deferens is the same gene which can cause cystic fibrosis. Cystic fibrosis is one of the most common genetic disorders and about one person in 25 is a carrier of one of the genes which causes it. To be affected by cystic fibrosis, a child would need to inherit one abnormal gene from both parents. It can be a very serious condition, causing a thick mucus to develop in the lungs which leads to repeated severe chest infections. Men with congenital absence of their vas deferens will be advised to have a blood test to check whether they are carrying a cystic fibrosis gene abnormality. More importantly, if the man's test shows he is a cystic fibrosis carrier, his partner will need to consider a screening test to check that, by chance, she is not a cystic fibrosis carrier as well. If she is, there may be a 1 in 4 chance of ICSI resulting in a child affected by cystic fibrosis and a 1 in 2 chance the child is themselves a carrier. A couple in this situation may wish to see a genetic counsellor and consider other options for fertility treatment.

Questions and concerns

We appreciate that many couples feel overwhelmed by the amount of information they receive about assisted conception treatments, particularly ICSI. It is always difficult to provide specific written information which covers the individual circumstances of every couple. We will be pleased to discuss any additional questions or concerns you may have either at your consultation or during the course of your treatment.

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