12.1.33.1 INFERTILITY TREATMENT FOR HIV DISCORDANT COUPLES WHERE THE MALE IS HIV POSITIVE

Introduction

The introduction of highly active antiretroviral treatment reduced the mortality rate from HIV infection in the USA in 1996 by 23%, with a further 47% reduction observed in 1997. The aim of this therapy is to the reduce HIV viral load in infected individuals to non-detectable levels. Once this has been achieved semen samples can be collected and tested for HIV RNA and DNA. Samples with non-detectable HIV can then be used for infertility treatments.

Transmission of the HIV virus during unprotected sexual intercourse

The rate of male to female transmission with unprotected intercourse is estimated to be approximately 1 per 1000, acts of unprotected intercourse, although this can range from 1 per 400 to 1 per 2000. Other research has suggested the risk may be greater. Some cases of transmission have been reported for those couples who have attempted pregnancy by having unprotected intercourse around the time of ovulation. In one report of 104 pregnancies in 92 women who conceived naturally, no transmissions were noted in the first three months of pregnancy, but two were noted at seven months and two after delivery. In another report of 92 couples where the male was HIV infected, six women became infected. The rate of viral transmission depends on many factors including, the stage of the disease and the viral load, with low levels of HIV load associated with lower risk of transmission.

Transmission of HIV to the child

The risk of viral transmission from an untreated HIV infected mother to the baby is 1:5, and if the mother is treated the risk is 1:12.5. With the use of antiviral therapy, caesarean section, and avoidance of breast feeding the risk of the child of an infected mother becoming infected is further reduced to less than 1 in 50.

Methods for reducing the risk of HIV transmission

Although there is **no** "risk-free" method of insuring safe conception for HIV discordant couples, recent advances in semen washing techniques used in conjunction with infertility treatment such as intrauterine insemination (IUI), in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) have been used to reduce the risk of vital transmission and have allowed many couples throughout the world where the male is HIV positive to achieve a pregnancy and deliver healthy children without viral transmission. Semen washing reduces the risk of viral transmission by removing everything from the semen except the sperm. Using fertility treatments such as IUI, IVF or ICSI further reduces the risk of transmission by limiting the number of sperm that an oocyte (egg) is exposed to.

12.1.33.2 INFERTILITY TREATMENT FOR HIV DISCORDANT COUPLES WHERE THE MALE IS HIV POSITIVE

Pioneering work in this area was done by Semprini and colleagues in the early 1990s. In the initial work, Semprini used a double semen washing technique in conjunction with IUI. Over 1000 inseminations were performed for 350 discordant couples resulting in 200 pregnancies. No transmission of HIV was reported. A decade later the results from 10 clinics in Europe were collated. To summarize this study 3,166 insemination procedure were performed on 1,263 HIV negative women, yielding 571 pregnancies and 393 births with no documented transmission of HIV to the women or children. Although these results are promising, with a transmission rate of approximately 1:1000 acts of unprotected intercourse it is difficult to demonstrate that IUI with washed sperm is safer than unprotected intercourse without information from a much larger number of cases.

Ideally for IUI to be effective 5 – 10 million sperm are washed and placed into the uterus, but with IVF or even ICSI the number of sperm needed for fertilization is in the thousands or a single sperm in the case of ICSI. Theoretically, this would act to further reduce the risk of viral transmission.

In 2003 researchers from Europe reported that of 125 IVF cases performed on 55 HIV discordant couples, 9 successful pregnancies were achieved. All women and babies tested negative for HIV. The same authors reported on 61 ICSI cycles that resulted in 22 ongoing pregnancies. At the time of publication no infections were reported in the women or children.

Risk of HIV transmission with infertility treatment

These results presented above are promising but at present there is **no** “risk free” method of conception where the male is infected with HIV. With semen washing and infertility treatment the risk of viral transmission is estimated to be less than 1 in 2000. This is a theoretical risk based on the idea that removing sperm from the potentially infectious cells in the semen will reduce the risk of viral transmission to below that of unprotected intercourse. Because a relatively small number of cases involving infertility treatment have been reported an accurate risk assessment cannot be provided at this point in time.

Theoretically, the risk of HIV transmission would be reduced if IVF / ICSI were used compared to IUI, as these treatments limit the number of sperm used and also avoid placing sperm directly into the uterus of the uninfected female partner as would occur with IUI.

Patients may choose in consultation with their clinician, the infertility treatment option most appropriate for them.

12.1.33.3 INFERTILITY TREATMENT FOR HIV DISCORDANT COUPLES WHERE THE MALE IS HIV POSITIVE

Protocol for minimizing the risk of HIV transmission during infertility treatment

Pre – Infertility treatment requirements
The male partner is required to have antiretroviral treatment under the care of a Clinical Immunologist. Secondly, the male must have undetectable HIV levels over at least two months, and semen samples at the end of this time with undetectable HIV RNA and DNA. The semen samples with undetectable HIV are cryopreserved (frozen) and stored for later use in IUI, IVF or ICSI procedures.

The female partner needs a referral to a Concept Fertility Specialist for routine gyneacological examination and preparation for IUI, IVF, or ICSI.

The couples are required to undergo counseling with regard to the risks and side effects of infertility treatments and the risks of viral transmission to the female partner and unborn child. This can be performed by Concept's Fertility Counselors and is available to all infertility patients without cost.
The couples are also required to provide written informed consent for the IUI, IVF or ICSI procedure as well as acknowledging an understanding of the risk of viral transmission.

Semen samples (3-6) for HIV testing and storage need to be collected at home by masturbation and transported (following instructions 12.2.6) to Royal Perth Hospital Immunology Department. The samples will then be processed using the double sperm washing technique to separate sperm from the seminal plasma. The sperm will be frozen and later tested for the presence of HIV. Semen samples with detectable HIV in the seminal plasma or sperm will be discarded and those with undetectable levels will remain in storage for subsequent use in infertility treatment cycles.

Infertility treatment Cycles
Treatment cycle management will be supervised by a Concept Clinician. Please refer to the following information sheets for specific details:
Introduction to Concept Fertility Centre (12.1.1)
Risks and Side Effects with drug treatments and surgery associated with ART (12.1.10)
Ovaries and Stimulation of Ovulation (12.1.4)
Infertility and Drugs (12.1.5)
Artificial Insemination Husband (12.3.1)
IVF Fact Sheet (12.3.5)
ICSI (12.3.8)

12.1.33.4 INFERTILITY TREATMENT FOR HIV DISCORDANT COUPLES WHERE THE MALE IS HIV POSITIVE

HIV monitoring for the female partner and child

It is important to closely monitor the female partner and child for HIV infection. The female partner therefore needs to be screened for HIV infection before commencing treatment, at day 10 of the treatment cycle, at the completion of the cycle, and after 3 months and 6 months. If pregnancy occurs, screening will be carried out at 4 weeks, 8 weeks, 26 weeks, 36 weeks, delivery and 6 weeks, 3 months, 6 months and 12 months after delivery. Children will be screened at birth, 3 months, 6 months, 12 months and then yearly for 5 years. This monitoring is under the care of the Clinical Immunologist who is managing the male partner's HIV infection.

If either the female partner or child becomes infected with HIV their infection would be treated by the Clinical Immunologist who is managing the male partner's HIV infection.

Risks of antiretroviral treatment during pregnancy

As with other drugs prescribed during pregnancy the potential risks for adverse side effects on the fetus or child depend on a number of factors including, the type of drug, the dose, the length of treatment, the stage of pregnancy and the genetic make-up of the mother and baby. The most widely used drug for treatment of HIV in pregnant women is zidovudine. Studies have shown that the only significant side effect was the presence of anemia in some infants. The anemia was mild and resolved quickly without the need for blood transfusion. There has been no evidence of an increase in abnormalities in infants exposed to zidovidine. Follow-up of children for over 4 years found no impact of the drug on growth or brain development. In a study of over 700 infants who were exposed to zidovidine, no cancers were observed up to six years of age.
Studies in animals suggest that some other drugs used to treat HIV infections may cause harm to the baby if taken during pregnancy. Patients are advised to discuss this with the Clinical Immunologist before commencing treatment.

It is Concept Fertility Centre policy to strictly adhere to universal infection control standard precautions in order to minimize the risk of transferring infection between patients or to our staff members. Details of these precautions are available on request.

For more information regarding this protocol please contact the Scientific Director at Concept Fertility Centre on 08 9382 2388.