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THE USE OF ASSISTED REPRODUCTION FOR HIV-INFECTED SERUM DISCORDANT COUPLES

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Abstract: The increase in longevity and quality of life has led serodiscordant couples to seek help in assisted reproduction, avoiding putting their partner at risk of infection or acquiring a new viral strain, being evaluated and treated on a case-by-case basis. There are inadequate data to prove that one therapy is safer than any other. In addition, the choice of treatment is based on available resources and the results of standard infertility tests, which are also part of the decision-making process. The general consensus in the legal and medical community is that HIV-infected couples or individuals must be counseled and have access to infertility treatment or treatment to decrease the risk of infection in an uninfected partner when attempting natural conception. HIV-infected patients seeking assisted reproduction services must be highly motivated to have children, well-controlled HIV with a stable CD4 count, undetectable virus in serum and semen (90 percent. When the woman is not HIV-infected and the If a man is infected with HIV, the risk of transmission is substantially reduced with the use of medically assisted reproduction. In women with a normal fertility assessment, intrauterine insemination (IUI) with doubly processed sperm as a first-line therapy is one of the options of choice. If unsuccessful or for couples diagnosed with known female factor infertility, in vitro fertilization (IVF) with intracytoplasmic sperm injection may be performed. Donated sperm is an additional option. When the woman is HIV-infected and the man is not is infected with HIV, IUI using the partner's sperm will prevent female-to-male transmission in an attempt to conceive Natural.

Keywords: Insemination, Serodiscordants, Assisted reproduction, Natural design, HIV, Hepatitis.

INTRODUCTION

A growing proportion of couples who seek fertility services have medical problems that need to be addressed, and being a complete family, from a cultural perspective, has led more and more couples with HIV or hepatitis C virus to seek out fertility services to understand how they can meet the need to become parents. From this perspective, the new family compositions defy science for the perpetuation of the species, without the transmission of viral pathologies that could compromise the future offspring, immediately or in the future, since these individuals can transmit the infection to an uninfected partner during the design process. Counseling these couples on the safest methods to prevent viral transmission to their partner involves discussing adoption, childlessness, and using a donor's sperm, in addition to natural or assisted conception with their own gametes. Among so many new forms of family, recognized by society, it is possible to specifically monitor serum discordant or serum concordance, in assisted reproduction, either in vitro or naturally. For a long time, techniques have been developed to assist in human perpetuation for uninfected couples, in an optimal situation of viral health, minimizing the risks, whatever they may be, for both parties, but there are also possibilities available for srodiscord, widely discussed in other countries, and lacking attention in Brazil. Other nations have managed to implement programs specifically applied to assisted reproduction in care of patients with immunocompromising viral pathologies, making sure that all guidelines are passed on by the multidisciplinary team in a humanized, correctly, ethically and respectfully manner, preserving the health of all. the parties involved, observing all the possibilities, pros, cons, risks of the technique, and even the possibility of not executing the technique, leaving for the adoption process. Recommendations for reducing the risk of viral transmission during fertility treatment were published by the American Society for Reproductive Medicine (ASRM). The basic principles underlying these recommendations are to reduce viral load in the infected partner(s), reduce uninfected partner exposure and susceptibility to infection, discuss available scientific evidence, and risk with the patient and their partner to provide a basis for informed consent. There is currently no ability to make an absolute recommendation for the best procedure to help serodiscordant couples to conceive because there are inadequate data to prove that any technique is significantly safer than any other and the choice of treatment is based on available resources and standard infertility test results, which are also part of the decision-making process. Assessment and treatment of patients is carried out on a case-by-case basis, always with the understanding that safer conception services are a critical component for couples affected by viral infections.

HIV INFECTION

The increase in longevity and quality of life has led HIV-infected individuals to think about long-term plans, such as having children. In a group of serodiscordant couples (where the man is living with HIV), 70 percent of couples expressed a desire to have children in the future if their fertility treatment was successful. Predictors of couples' desires for additional children if fertility treatment is successful were younger age, shorter duration of relationship, not currently having children, and having the male partner's HIV diagnosis known before the couple met. Therefore, it is important to understand the general fertility desires in this patient population, in combination with a discussion of the various methods by which pregnancy can be achieved. Men and women living with HIV can seek

help with pregnancy planning to avoid unprotected sex with an uninfected partner when the couple is trying to conceive. A survey in the United States reported that 12 percent of HIV serodiscordant couples concerned about transmitting HIV to their partner would still be willing to have unprotected sex if there were no other alternatives to achieving pregnancy (KLEIN et al., 2003). Ideally, these couples must have an alternative to unprotected intercourse because even partners with undetectable plasma levels of HIV can transmit HIV in semen, female genital secretions, and rectal secretions (Centers for DiseaseControlandPrevention–CDC, 2003). However, the risk of transmission appears to be very low when the HIV-infected partner is receiving maximally suppressed antiretroviral therapy (CASTILLA et al., 2006).

INITIAL ASSESSMENT

Treatment of HIV-infected patients with a desire to become pregnant involves a multidisciplinary approach, ideally including specialists in maternal-fetal medicine, HIV specialists, neonatologists, pediatricians, psychiatrists, social workers, and reproductive endocrinologists. A team of providers knowledgeable in this area must review each case, including the couple's ability to tolerate fertility assessment, treatment, and pregnancy. Access to an institution that can care for pregnant patients with HIV and the child born under these circumstances is also a prerequisite for initiating fertility treatment. In addition, program staff must be trained on how to process samples and separate freezing facilities for gametes/embryos from HIV-infected clients. While the 2015 American Society for Reproductive Medicine committee opinion found "no ethical reason to suspend fertility services," access to assisted reproductive technology services for HIV-infected individuals remains variable and appears to differ based on who does the research (EthicsCommittee of American Society for Reproductive Medicine, 2015).

In a survey of 140 infertility clinics in the United States, when a clinician asked about assisted reproductive technology services for an HIV-infected individual, 63 percent of clinics offered services to a couple with an HIV-infected man and a non-HIV-infected woman. infected by HIV; however, when the caller was identified as a patient, only 40 percent offered services. Of clinics that do not provide services to patient callers, only half (51 percent) referred patients to other clinics, further demonstrating the need to overcome barriers to accessing assisted reproductive technology in this population (LEECH et al., 2018).

HIV-infected couples seeking fertility treatment must undergo a medical evaluation, where the medical status of both partners must be assessed, appropriate preventive therapies must be initiated, and any issues that can be treated must be addressed by their primary care provider. and/or HIV specialist before starting fertility therapy. They must also undergo an assessment of possible antiretroviral therapy, with an assessment of the need for antiretrovirals and other medical therapies. Some questions that need to be addressed by the HIV specialist are: Must the patient start antiretroviral therapy if they are not already taking these drugs? Is he/she in the ideal regime? Must an HIV-uninfected partner of an HIV-infected man receive prophylactic antiretroviral therapy during assisted reproductive technology? In the United States, initiation of antiretroviral therapy is recommended for all HIV-infected individuals to reduce the risk of HIV and non-HIV-related morbidity and mortality (Panelon Antiretroviral Guidelines for Adults and Adolescents, 2020).

Antiretroviral therapy can also be helpful from a fertility point of view as well as a medical point of view. Some experts believe it can improve the outcome of sperm washing/intrauterine insemination (IUI), while others do not (NICOPOULLOS et al., 2009). Although routine semen analysis may not be significantly different between HIV-infected and uninfected men, as HIV infection progresses, semen parameters show decreased concentration, motility, and number of normal morphological sperm and increased round cells with more viscous semen (NICOPOULLOS et al., 2004). There is probably a positive correlation between total sperm concentration and CD4 cell count (DULIOUST et al, 2002). A retrospective study describing observations from 10 years of experience providing fertility care to HIV-infected men reported that 76 of 181 of these men (42 percent) had an abnormal semen analysis with at least one parameter in the subfertile range (SAUER et al., 2009). In a retrospective case-control study of 770 men using highly active antiretroviral therapy (HAART), mean values of all semen parameters were statistically lower for HIV-1 infected individuals compared to the World Organization reference group. of Health (WHO) 2010 (SAVASI et al., 2019). Semen analysis parameters below the 5th percentile of the WHO reference group occurred in 26 percent of the volume group, 32 percent for progressive motility and 28 percent for normal morphology. Theories for sperm alterations include poor spermatogenesis, ejaculatory dysfunction, prostate/seminal vesicle dysfunction, increased reactive oxygen species, or Leydig cell dysfunction due to the interaction of infected macrophages with degeneration of the seminal epithelium (NICOPOULLOS et al., 2004).

Fertility Assessment – Before undergoing time-consuming, expensive, and complex treatments such as IUI or in vitro fertilization (IVF), factors that may affect outcomes are assessed, even if the HIV-infected patient or their partner is not infertile. This assessment includes:

- Semen analysis. Leukocytospermia must be evaluated. If present, it can increase the risk of HIV transmission. Semen parameters affect the choice of treatment. (KALU et al., 2010).
- Assessment of ovulatory function and ovarian reserve. (KALU et al., 2010).
- Evaluation of the permeability of the fallopian tubes. HIV-infected women are at risk of tubal disease infertility given the increased prevalence of other sexually transmitted infections in HIV-infected individuals. al., 2010).
- Uterine cavity assessment. Uterine evaluation is performed if clinically indicated.

Hysterosalpingography, sonohysterography, or hysteroscopy is performed before IVF to ensure that there are no abnormalities that could interfere with pregnancy, such as submucosal fibroids or uterine septum (KALU et al., 2010). HIV infection appears to affect fertility parameters in both women and men. A review of age-specific fertility rates (ASFR) from demographic and health surveys revealed a decreasing fertility rate among HIV-infected women compared with HIV-uninfected women (CHEN; WALKER, 2010). The ASFR is calculated as the total number of births in the 36 months preceding the survey, divided by the sum of the woman's years of childbearing age during those 36 months, multiplied by 1000 for each five-year range. The ASFR ratio (defined as a proportion of ASFRs of HIV-infected women divided by ASFRs of HIV-uninfected women) for each 15-49 five-year-old age group was 1.2, 0.77, 0, 71, 0.65, 0.59, 0.53, 0.47. In addition, a case-control study reported lower anti-Müllerian hormone levels for women with HIV compared to uninfected control women

(3.0 ± 2.8 versus 3.7 ± 3.5 ng/mL, respectively) (SANTULLI et al., 2016).

However, the clinical significance of this difference is not yet known. A different case-control study reported a lower clinical pregnancy rate per transfer, although implantation and live birth rates per transfer were not significantly different between HIV-infected women compared to controls (STORA et al., 2016). For HIV-infected men, semen testing (especially those using antiretroviral therapy) revealed a lower ejaculate volume, decreased sperm motility, and increased abnormal sperm morphology compared to controls (KEHL et al., 2015).

COUNSELING AND EVALUATION

Patients are counseled about the psychosocial factors involved in seeking fertility treatment and are assessed to ensure they understand and accept these risks. The exact method of conception must be decided after careful discussion with HIV and reproductive experts (BUJAN; PASQUIER, 2016).

Ideal candidates for Fertility Services - Experts have suggested the following criteria to guide clinicians in the selection of HIV-infected patients seeking assistance for conception:

- High motivation to have children;
- Well controlled HIV with stable CD4 count;
- Undetectable virus in serum and semen (90%) (WILLIAMS et al., 2009).

HIV-INFECTED MAN AND HIV-UNINFECTED WOMAN

The goal when a man is infected is to prevent transmission of the infection to his partner and fetus. Options include using donor sperm, IUI using prepared (washed) sperm from the infected man, or in vitro fertilization (with intracytoplasmic sperm injection – ICSI) using prepared (washed) sperm from the infected man. The male partner must be receiving antiretroviral therapy and ideally demonstrate sustained suppression of plasma viral load below detection limits (Recommendations for use ofantiretroviraldrugs in pregnanthiv-1-infected women for maternal healthandinterventionstoreduce perinatal hivtransmission in theUnited States, 2020).

DONOR INSEMINATION

The use of donor sperm from an HIV-uninfected man and IUI is the safest option for HIV-uninfected women desiring conception. If the couple decides to use a donor's sperm, they must be informed that a donor's sperm samples are quarantined for at least 180 days (i.e. six months) after the date of donation to allow for testing and donor retesting for communicable diseases such as HIV (Recommendations for use of antiretroviral drugs in pregnant hiv-1-infected women for maternal health and interventions to reduce perinatal hiv transmission in the United States, 2020).

INTRAUTERINE INSEMINATION WITH PROCESSED SPERM

For couples who do not wish to use donor sperm, sperm preparation techniques (ie, sperm washing) combined with IUI or IVF are options to limit the risk of transmitting HIV to the uninfected partner. The rationale for this approach, even when there is no detectable virus in the man's serum, comes from data reporting that semen can contain a high viral load and transmission to a partner can occur (Centers for Disease Control and Prevention – CDC, 2003). The risk of female seroconversion is likely to be substantially reduced with the use of medically assisted reproduction. In couples with a normal fertility assessment, IUI with specially processed sperm is a safe and effective strategy (BARNES et al., 2016).

Some specialists also treat the partner with pre-exposure prophylaxis (PrEP) at the time of IUI with washed sperm. In a study of 11 serodiscordant couples who underwent 28 cycles of IUI using washed sperm combined with PrEP, six cycles resulted in pregnancy (21 percent fertility rate), and all women remained HIV seronegative at six months of follow-up. for couples in which semen analysis is abnormal, IVF may be the best treatment option (SAFIER et al., 2017). It has been suggested that HIV is carried in seminal fluid and white blood cells and that sperm are not carriers of the virus because they lack the necessary viral receptors, but this is controversial. Most authorities believe that sperm does not contain HIV on its surface or in the cell. However, it is easy to contaminate a sperm preparation with microscopic amounts of semen. Washing sperm before IUI eliminates round cells, seminal plasma, and most immobile sperm.

Sperm are isolated by sequential density gradient and swimming techniques and are then tested by PCR assays for the presence of HIV RNA. Using this method of sperm preparation, less than 1 percent of sperm samples from HIV-infected men test positive (typically, these "positives" are "low level" positive tests). A Cochrane review noted, however, that there were no relevant clinical trials identified in the literature to determine the benefits and risks of sperm washing to prevent HIV transmission in the attempted conception setting (EKE; ORAGWU, 2011).

The purpose of IUI is to place "virus-free" sperm into the uterine cavity close to the time of ovulation. If the PCR tests are negative for HIV, the sperm are transferred into the uterine cavity through a flexible catheter. Using this protocol over several thousand cycles, there was a zero rate of seroconversion in female partners and no documented births of HIV-infected children (VITORINO et al., 2011). However, couples must be warned that the risk of acquiring HIV from insemination with prepared (washed) sperm from an HIV-infected partner has not yet been definitively proven to be zero. We may be getting closer to guaranteeing a transmission rate of zero with the advent of nested PCR, which can detect a single viral copy of HIV (MESEGUER et al., 2002).

IVF WITH ICSI

Intrauterine insemination has been the traditional medical approach to achieving conception in discordant couples because of its convenience and low cost. Since this approach still leaves the potential for thousands to millions of sperm and possible remnants of HIV from the seminal fluid to come into contact with the partner, the use of IVF with ICSI has growing appeal, even when there is no evidence from women or male infertility factors (SAUER et al., 1998).

IVF with ICSI is used as a first-line approach when there are insufficient sperm for IUI or, theoretically, to reduce exposure to the virus. The combination of sperm washing in this PCR and ICSI potentially has several advantages (GARRIDO et al, 2005): •Provides minimal sperm exposure and seminal/ prostatic secretion (a single sperm for each oocyte); •Disease-negative sperm samples are now available to the patient for future cycles if the sperm are cryopreserved; •Sperm washing is performed before the cycle so that cycles are not canceled due to a positive PCR test result; •There is no need to recover large numbers of sperm to achieve adequate pregnancy rates after washing (as in IUI); •Pregnancy rates are more than three times higher than for IUI; •A higher pregnancy rate decreases the number of attempts and exposures (GARRIDO et al., 2005). Pregnancy rates after ICSI in serodiscordant couples are similar to those of HIV-uninfected couples undergoing ICSI

(SAUER et al., 2011). No seroconversion over 700 cycles has been documented using the ICSI IVF approach (VITORINO et al., 2011).

However, as with IUI, prevention of viral transmission of HIV cannot be guaranteed. Although IVF with ICSI theoretically reduces a woman's exposure to the virus, there are several reasons why it is not the standard technique for all HIV-discordant couples. For example, pregnancies conceived through IVF are associated with increased risks of multiple pregnancies, congenital anomalies, preterm birth, low birth weight, and the complications associated with these outcomes. Furthermore, the IVF process, which involves ovulation induction, egg retrieval, and embryo transfer, is not a risk-free surgical procedure and is expensive.

Potential complications include bleeding, infection and damage to the bowel, bladder, blood vessels and other internal organs/structures. Thus, while minimizing transmission of the virus is a major concern in decision-making for these couples, it is not the only concern. There is a theoretical risk of contamination of the oocyte or embryo by HIV during in vitro fertilization procedures (GILLING-SMITH et al., 2006). After IVF/ICSI because of paternal HIV infection, no births of HIV-infected children from uninfected mothers have been documented (VITORINO et al., 2011).

HIV-INFECTED WOMAN AND HIV-UNINFECTED MAN

The objective in this situation is to prevent transmission of the virus to humans. For these couples, the safest form of conception is artificial insemination, including the option for the woman to self-inseminate herself with her partner's sperm during the periovulatory period. and Interventions to Reduce Perinatal HIV Transmission in the United States, 2020). A meta-analysis reported that pregnancy rates are generally similar to those of HIV-uninfected couples undergoing IUI, but may be lower for assisted reproductive technology; however, this requires further study, as several factors may be responsible for the discrepancy (BARNES et al., 2014).

Compared with HIV-uninfected women, HIV-infected women who discontinued contraception with the intention of becoming pregnant had decreased fertility (defined as the time to pregnancy within 12 months of stopping contraception); differences of 25 to 40 percent have been reported (LEWIS et al., 2006).

INTRAUTERINE INSEMINATION (IIU)

IUI using the male partner's sperm will avoid exposing the man to his partner's vaginal secretions. If IUI is not successful or if there is severe male factor infertility, IVF can be performed according to usual protocols (VITORINO et al., 2011). The following is a low-cost, low-resource alternative approach to IUI: •The timing of peak luteinizing hormone (LH), which means imminent ovulation, is determined using an ovulation predictor kit; •When the LH surge is identified, the man ejaculates in a condom without spermicide; •A syringe (without needle) is then used to aspirate the semen into the condom; •The syringe is inserted into the vagina and the semen is released close to the cervix (VITORINO et al., 2011).

FIV (FERTILIZATION *IN VITRO*)

Like IUI, the use of IVF prevents contact between an HIV-uninfected man and an HIV-infected woman. If IVF is performed, HIV-infected women may have a clinically varied response to ovarian hyperstimulation. One study reported that only the CD4 cell count of HIV-infected women had an effect on the occurrence of ovarian resistance to IVF-

stimulating drugs and that increased amounts of gonadotropins were required to result in ovarian hyperstimulation in HIV-infected women (COLL et al. al., 2006). It is unclear whether HIV infection affects the outcome of assisted reproductive technology, particularly in vitro fertilization. In a systematic review of 10 studies including 342 HIV-infected women, ovarian stimulation cancellation rates were higher and pregnancy rates were lower for HIV-infected women compared to uninfected women (MARQUES; GUERREIRO; SOARES, 2015).

Multiple pregnancies are more problematic for HIV-infected women because these pregnancies carry a higher risk of preterm delivery. Prematurity, related to multiple pregnancy and possibly antiretroviral therapy (particularly those containing protease inhibitors), together with obstetric complications increase the risk of maternal-fetal transmission of HIV (SCAVALLI et al., 2007). For these reasons, single-embryo transfer is desirable in this population (especially in women <40 years) (OHL et al., 2005).

NATURAL CONCEPTION IN SERODISCORDANT COUPLES

Although successful antiretroviral therapy from the infected partner dramatically reduces the rate of HIV transmission in serodiscordant couples, it is uncertain whether it can completely eliminate the risk (ANGLEMYER et al., 2013). In addition, transmission can occur despite antiretroviral use, when infected individuals have not achieved viral suppression during therapy. Furthermore, two out of three HIV-affected couples experience subfertility and may benefit from early recognition of fertility factors (IYER et al., 2019). For serodiscordant couples who wish to become pregnant, several steps can be taken before attempting conception to reduce the risk of transmitting HIV to the uninfected partner (Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States, 2020):

- Both partners must be screened and treated for genital tract infections (MATTHEWS et al., 2011).
- The HIV-infected partner must be receiving combination antiretroviral therapy and demonstrate sustained suppression of plasma viral load below detection limits (MATTHEWS et al., 2011).
- PrEP for the HIV-uninfected partner may further reduce the risk of sexual transmission (MATTHEWS et al., 2011). Because of these uncertainties, it is prudent to continue to recommend safe sexual practices (i.e. condom use) and the use of assisted reproduction techniques until more information on optimal management of these couples is available (Recommendations for use of antiretroviral drugs in pregnant hiv-1- infected women for maternal health and interventions to reduce perinatal hiv transmission in the United States, 2020).

The benefit of PrEP to the HIV-uninfected partner, other than suppressing viral load below the detectable threshold in the HIV-infected partner, is not known. The use of PrEP peri-conception and subsequent continued use during pregnancy is acceptable and feasible for those desiring a pregnancy. It offers autonomy as a use-controlled prevention technique in the peri-conception period for women and men (HEFFRON et al., 2016). In addition to optimal medical suppression of the HIV-infected partner, serodiscordant couples must time unprotected intercourse to coincide with ovulation to maximize the chance of pregnancy and minimize the number of exposed sexual events. In a case series of 46 couples in which the HIV-infected male

partner was on optimal suppressive therapy for at least six months, the cumulative pregnancy rate was 66 percent after five attempts, and no seroconversion occurred (VERNAZZA et al.., 2011). Scheduled intercourse also appears beneficial for couples in which the HIV-infected partner may have a detectable viral load. A study of HIV-uninfected women who had scheduled sex with HIV-infected partners (whose CD4 counts ranged from 7 to 1273/microL; viral loads were not available) reported that 4 of 92 (4.3 percent) seroconverted. No seroconversion occurred in the first three months after conception, but two women seroconverted in the third trimester and two seroconverted postpartum. All four seroconversions occurred in couples who reported inconsistent condom use (MANDELBROT et al., 1997).

SEROCONCORDANT COUPLES

If both partners are infected, the couple may be worried about acquiring a new viral strain of the disease from their partner. It has been hypothesized that assisted reproductive technology may be useful in these couples to decrease the risk of transmitting a different or mutated strain to the partner. If one partner has a single viral mutation, IUI will reduce the risk of transmission to the male partner. If the male partner has the single mutation, then sperm washing or donor insemination can be used to reduce the woman's risk of acquiring the mutated virus. However, most couples do not know what subtype of HIV they are carrying. Furthermore, there are no data to document the magnitude and clinical implications of transmission of genotypically divergent strains through sexual intercourse or assisted reproductive technology between HIV-infected, subtype-discordant partners. Therefore, these questions are of theoretical interest, but do not influence treatment recommendations with assisted reproductive technology at this time. Most of these couples try to conceive naturally. If infertility problems arise, they will be treated in the same way as in uninfected couples. Of note, a study of 85 HIV-infected couples undergoing assisted reproductive technology reported lower rates of ongoing pregnancy when both partners were HIV positive (MANIGART et al., 2006). A subsequent retrospective case-control study also described a poor IVF pregnancy outcome for seroconcordant couples, with only one delivery occurring in 33 IVF cycles. age, previous history of advanced HIV disease (which may affect fertility), or by chance (VANKERKEM et al., 2017).

LEGAL AND ETHIC ISSUES

The general consensus in the medical (Ethics Committee of the American Society for Reproductive Medicine. 2010) and legal communities caring for HIV-infected individuals is that these individuals must be counseled and have access to infertility treatment or treatment to decrease the risk of infection. in an uninfected partner when the couple is trying to conceive (PHELPS, 2007). Physicians must have the right to assist infertility patients with HIV in their reproductive goals, without fault if a child is affected (PENNINGS, 2003). After appropriate evaluation, however, some patients may not be candidates for assisted reproductive technology and the physician is not legally obligated to provide the treatment. In couples with HIV, assistance in conceiving children is supported by the following (Ethics Committee of the American Society for Reproductive Medicine, 2010): •The prognosis of HIV patients has significantly improved with antiretroviral therapy, allowing HIV-infected patients to be considered along a continuum of chronic disease. •Perinatal transmission has significantly decreased with medical interventions. •Assisted reproductive

technology appears to enable HIV-discordant couples to decrease the risk of viral transmission to the unaffected partner. On the other hand, opponents of offering infertility treatment to these individuals make the following points (American College of Obstetrics and Gynecology. 2007): •The parents' prognosis is uncertain; it may not be in the child's best interest to be born to a parent who may not be available to provide long-term care for that child. •There is a risk that the child will contract HIV from the parents. This risk is lower than before medical and surgical interventions to prevent perinatal transmission, but not zero. •Toxicity and risk of antiretroviral therapy are considered minimal, but these issues have not been fully elucidated. •Theoretically, the development of drug resistance can be enhanced by administering prophylactic regimens of antiretroviral agents to prevent perinatal transmission to many women who would not be considered for drug therapy in the absence of pregnancy (FRODSHAM, 2004).

Legal issues

Bragdon versus Abbott and the American Disabilities Act (ADA) suggest that individuals with HIV may be classified as disabled and entitled to medical care unless objective scientific evidence is available that a "significant risk" with the proposed treatment is present (BRAGDON; ABBOTT, 1998). According to the ADA, "no individual shall be discriminated against on the basis of disability in full and equal enjoyment of accommodations in any public accommodation," which includes the "professional office of a health care provider." Handling samples from HIV-infected patients poses a risk to the health and safety of others, but this risk can be reduced or eliminated by universal precautions and separate storage facilities. Therefore, HIV-infected status is not sufficient to justify discontinuation of infertility treatment (The American with Disabilities Act, 1990). Harm can also be thought of in terms of "wrong birth" and "wrong life". Unfair life occurs when the child claims that neglect has occurred and that no life would be superior to the current one (ELSTER, 2003). The unjust life is similar to the ethical principle of non-maleficence (first, do no harm). Parents can claim the wrongful birth against a healthcare professional who does not fully inform them of the possibility of the mother having a child with an illness. This reinforces the importance of a broad process of informed consent that allows the patient's autonomy in the decision to proceed with the treatment with the understanding of the possibility of transmission of HIV to the child. If both partners are infected, then the child's well-being must be considered.

Ethical issues

The Ethics Committee of the American College of Obstetricians and Gynecologists has stated that there is an ethical obligation to provide assisted reproductive technology to couples where one or both partners are infected with HIV, while respecting patient autonomy and fetal beneficence (American College of Obstetrics and Gynecology), 2007). The Ethics Committee of the American Society for Reproductive Medicine (ASRM) has indicated that healthcare professionals may be legally and ethically obligated to provide requested assistance for reproduction. This committee opinion on HIV and infertility treatment notes that there is no ethical reason to suspend fertility services for HIV-infected individuals, and clinics lacking sufficient resources to provide care must refer patients to appropriate providers who can offer treatment options. (Ethics Committee of the American Society for Reproductive Medicine, 2015). In 2010, the California Department of Public Health mandated that all fertility centers

provide appropriate fertility interventions for HIV-infected individuals seeking infertility care, or refer the couple to a center that offers such services. As discussed above, opponents of providing assisted reproductive technology to HIV serodiscordant or seroconcordant couples have cited the severity of the illness, the availability of reproductive alternatives, and the best interests of the child (ZUTLEVICST, 2006). These arguments were refuted, based on the following principles:

•Autonomy – it reflects the patient's choice, after all information is provided, to continue with infertility treatment despite one or both partners being HIV infected. When considering HIV, it is helpful to point out other disease processes for which we do not deny access to infertility assessment/ treatment. Many couples with autosomal recessive disorders such as cystic fibrosis and Tay-Sachs have a 25% chance of passing the disease on to their children. These diseases can also lead to infant mortality, but they carry a higher risk of transmission than HIV, and yet we allow these couples to proceed with infertility treatment after appropriate genetic counseling. In addition, women with chronic diseases such as diabetes and heart disease, where pregnancy can affect the health of the mother (GILLING-SMITH; SMITH; SEMPRINIAE, 2001). •Beneficence – It is the health professional's obligation to promote the health of their patients. Doctors can help patients lessen the transmission of the HIV virus to their partner and can help provide the couple with the psychological well-being that comes from the joy of having a genetically related child. The benefit of a supportive medical environment can encourage a woman to obtain medical and antenatal care and take precautions to prevent transmission to her child (GILLING-SMITH, 2001). •Justice – it refers to the battle between the right to reproduction and the possibility of an affected child to suffer and whose care has economic and social implications for the society in which they live (WILLIAMS; FINNERTY; NEWBERRYYG; 2003).

FINAL CONSIDERATIONS

Current information bases are derived from observational studies that demonstrate the need for further research with a multicenter randomized trial in this area. As there has been no documented transmission of HIV through any processing method currently used, it is unclear how randomization to treatment other than sperm washing can be ethically performed. The immunological tests carried out so far express a great need to research even more on how to generate greater quality and safety for assisted reproduction for these patients, who show a great desire to reproduce naturally, given the drug safety that exists today in day. Patients living with HIV and undergoing regular treatment, who maintain their viral load undetectable, and do not present risky behavior, generating reinfections, acquiring new strains and promoting new viral mutations, end up being submitted to a large battery of exams so that there is certainty of the protection of the same and of his/her partner in order to reproduce, whether natural or assisted, guarantees success for both parties, doctor and patient. Assisted reproduction clinics guarantee a large part of the research process and correct performance of oocyte and sperm analysis techniques. The technology applied to assist in treatments is also of great importance when choosing the best method of monitoring the assisted reproduction process. The risk is best justified by the low rate of perinatal transmission (less than 2 percent with adequate precautions), which is lower than the general population risk of congenital malformations of medical, surgical, or cosmetic significance (3% to 5%).

REFERENCES

Ahmed MM, Huang TH, Xie QD. **A sensitive and rapid assay for investigating vertical transmission of hepatitis B virus via male germ line using EGFP Vector as reporter.** J Biomed Biotechnol 2008; 2008:495436.

Alter MJ, Hadler SC, Margolis HS, et al. **The changing epidemiology of hepatitis B in the United States. Need for alternative vaccination strategies.** JAMA 1990; 263:1218.

American College of Obstetrics and Gynecology. ACOG Committee Opinion No. 389, December 2007. **Human immunodeficiency virus.**ObstetGynecol 2007; 110:1473.

Anglemyer A, Horvath T, Rutherford G. **Antiretroviral therapy for prevention of HIV transmission in HIV-discordant couples.** JAMA 2013; 310:1619.

Anglemyer A, Rutherford GW, Horvath T, et al. **Antiretroviral therapy for prevention of HIV transmission in HIV-discordant couples.** Cochrane Database Syst Rev 2013; CD009153.

Barnes A, Riche D, Mena L, et al. **Efficacy and safety of intrauterine insemination and assisted reproductive technology in populations serodiscordant for human immunodeficiency virus: a systematic review and meta-analysis.** Fertil Steril 2014; 102:424.

Barreiro P, del Romero J, Leal M, et al. **Natural pregnancies in HIVserodiscordant couples receiving successful antiretroviral therapy.** J Acquir Immune Defic Syndr 2006; 43:324.

Beasley RP, Hwang LY, Lin CC, et al. **Incidence of hepatitis B virus infections in preschool children in Taiwan.** J Infect Dis 1982; 146:198.

Bourlet T, Lornage J, Maertens A, et al. **Prospective evaluation of the threat related to the use of seminal fractions from hepatitis C virus-infected men in assisted reproductive techniques.** Hum Reprod 2009; 24:530.

Bragdon v. Abbott, in 524. 1998, U.S. 624.

Bujan L, Pasquier C. **People living with HIV and procreation: 30 years of progress from prohibition to freedom?**Hum Reprod 2016; 31:918.

Carosi G, Nasta P, Fiore S, et al. **Womenfacing HIV. Key question on women with HIV infection: Italian consensus workshop. Infection** 2009; 37:168.

Castilla J, Del Romero J, Hernando V, et al. **Effectiveness of highly active antiretroviral therapy in reducing heterosexual transmission of HIV**. J Acquir Immune Defic Syndr 2005; 40:96.

Centers for Disease Control and Prevention (CDC), Health Resources and Services Administration, National Institutes of Health, HIV Medicine Association of the Infectious Diseases Society of America. Incorporating HIV prevention into the medical care of persons living with HIV. Recommendations of CDC, the Health Resources and Services Administration, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. MMWRRecomm Rep 2003; 52:1.

Centers for Disease Control and Prevention. Viral Hepatitis Surveillance – United States, 2018. https://www.cdc.gov/hepatitis/statistics/SurveillanceRpts.htm. Published July 2020. (Accessed on August 23, 2020).

Centers for Disease Control. Surveillance for viral hepatitis – United States, 2013 http://www.cdc.gov/hepatitis/statistics/2013surveillance/commentary.htm#hepatitisB (Accessed on October 02, 2015).

Chen WJ, Walker N. **Fertility of HIV-infected women: insights from Demographic and Health Surveys. Sex Transm Infect** 2010; 86 Suppl 2:ii22.

Coll O, Suy A, Figueras F, et al. **Decreased pregnancy rate after in-vitro fertilization in HIV-infected women receiving HAART.** HIV 2006; 20:121.

Douglas NC, Wang JG, Yu B, et al. **A systematic, multidisciplinary approach to address the reproductive needs of HIV-seropositive women**. Reprod Biomed Online 2009; 19:257.

Dulioust E, Du AL, Costagliola D, et al. **Semen alterations in HIV-1 infected men. Hum Reprod** 2002; 17:2112.

Eke AC, Oragwu C. **Sperm washing to prevent HIV transmission from HIVinfected men but allowing conception in serodiscordant couples.** Cochrane Database Syst Rev 2011; :CD008498.

Elster NR. **HIV and art: reproductive choices and challenges**. J Contemp Health Law Policy 2003; 19:415.

Englert Y, Moens E, Vannin AS, et al. **Impaired ovarian stimulation during in vitro fertilization in women who are seropositive for hepatitis C virus and seronegative for human immunodeficiency virus.** Fertil Steril 2007; 88:607.

Ethics Committee of American Society for Reproductive Medicine. Human immunodeficiency virus (HIV) and infertility treatment: a committee opinion. Fertil Steril 2015; 104:e1.

Ethics Committee of the American Society for Reproductive Medicine. Human immunodeficiency virus and infertility treatment. Fertil Steril 2010; 94:11.

Frapsauce C, Grabar S, Leruez-Ville M, et al. **Impaired sperm motility in HIVinfected men: an unexpected adverse effect of efavirenz?** Hum Reprod 2015; 30:1797.

Frodsham LC, Smith JR, Gilling-Smith C. **Assessment of welfare of the child in HIV positive couples.** Hum Reprod 2004; 19:2420.

Garrido N, Meseguer M, Bellver J, et al. **Report of the results of a 2 year programme of sperm wash and ICSI treatment for human immunodeficiency virus and hepatitis C virus serodiscordant couples.** Hum Reprod 2004; 19:2581.

Gilling-Smith C, Nicopoullos JD, Semprini AE, Frodsham LC. **HIV and reproductive care--a review of current practice.**BJOG 2006; 113:869.

Gilling-Smith C, Smith JR, Semprini AE. **HIV and infertility: time to treat. There's no justification for denying treatment to parents who are HIV positive.**BMJ 2001; 322:566.

Goh KT. **Prevention and control of hepatitis B virus infection in Singapore.** Ann Acad Med Singapore 1997; 26:671.

Gosselin JT, Sauer MV. Life after HIV: examination of HIV serodiscordant couples' desire to conceive through assisted reproduction. HIV Behav 2011; 15:469.

Hanson BM, Dorais JA. **Reproductive considerations in the setting of chronic viral illness.** Am J ObstetGynecol 2017; 217:4.

Harris AM, Iqbal K, Schillie S, et al. Increases in Acute Hepatitis B Virus Infections - Kentucky, Tennessee, and West Virginia, 2006-2013. MMWRMorb Mortal Wkly Rep 2016; 65:47.

Heffron R, Pintye J, Matthews LT, et al. **PrEP as Peri-conception HIV Prevention for Women and Men.**Curr HIV Rep 2016; 13:131.

Iqbal K, Klevens RM, Kainer MA, et al. **Epidemiology of Acute Hepatitis B in the United States From Population-Based Surveillance, 2006-2011.** Clin Infect Dis 2015; 61:584.

Iyer JR, Van Rie A, Haberlen SA, et al. **Subfertility among HIV-affected couples in a safer conception cohort in South Africa.** Am J ObstetGynecol 2019; 221:48.e1.

Kaida A, Andia I, Maier M, et al. **The potential impact of antiretroviral therapy on fertility in sub-Saharan Africa.**Curr HIV Rep 2006; 3:187.

Kalu E, Wood R, Vourliotis M, Gilling-Smith C. **Fertility needs and funding in couples with blood-borne viral infection.** HIV Med 2010; 11:90.

Karampatou A, Han X, Kondili LA, et al. **Premature ovarian senescence and a high miscarriage rate impair fertility in women with HCV.** J Hepatol 2017.

Kehl S, Weigel M, Müller D, et al. **HIV-infection and modern antiretroviral therapy impair sperm quality.** Arch GynecolObstet 2011; 284:229.

Kim WR, Ishitani MB, Dickson ER, et al. **Rising burden of hepatitis B in the United States: Must the other virus be forgotten?** (abstract). Hepatology 2002; 36:222A.

Klein J, Peña JE, Thornton MH, Sauer MV. **Understanding the motivations, concerns, and desires of human immunodeficiency virus 1-serodiscordant couples wishing to have children through assisted reproduction.**ObstetGynecol 2003; 101:987.

Lampe MA, Smith DK, Anderson GJ, et al. **Achieving safe conception in HIVdiscordant couples: the potential role of oral preexposure prophylaxis (PrEP) in the United States.** Am J ObstetGynecol 2011; 204:488.e1.

Leech AA, Bortoletto P, Christiansen C, et al. **Assessing access to assisted reproductive services for serodiscordant couples with human immunodeficiency virus infection.** Fertil Steril 2018; 109:473.

Levy R, Tardy JC, Bourlet T, et al. **Transmission risk of hepatitis C virus in assisted reproductive techniques.** Hum Reprod 2000; 15:810.

Lewis JJ, Ronsmans C, Ezeh A, Gregson S. **The population impact of HIV on fertility in sub-Saharan Africa.** HIV 2004; 18 Suppl 2:S35.

Lin CL, Kao JH, Chen BF, et al. **Application of hepatitis B virus genotyping and phylogenetic analysis in intrafamilial transmission of hepatitis B virus.** Clin Infect Dis 2005; 41:1576.

Loutradis D, Drakakis P, Kallianidis K, et al. **Birth of two infants who were seronegative for human immunodeficiency virus type 1 (HIV-1) after intracytoplasmic injection of sperm from HIV-1-seropositive men.** Fertil Steril 2001; 75:210.

Mandelbrot L, Heard I, Henrion-Géant E, Henrion R. **Natural conception in HIVnegative women with HIV-infected partners.** Lancet 1997; 349:850.

Manigart Y, Rozenberg S, Barlow P, et al. **ART outcome in HIV-infected patients.**Hum Reprod 2006; 21:2935.

Marina S, Marina F, Alcolea R, et al. **Human immunodeficiency virus type 1-serodiscordant couples can bear healthy children after undergoing intrauterine insemination.**FertilSteril 1998; 70:35.

Marina S, Marina F, Alcolea R, et al. **Pregnancy following intracytoplasmic sperm injection from an HIV-1-seropositive man.**Hum Reprod 1998; 13:3247.

Marques C, Guerreiro C, Soares SR. **Lights and Shadows about the Effectiveness of IVF in HIV Infected Women: A Systematic Review.** Infect Dis ObstetGynecol 2015; 2015:517208.

Matthews LT, Baeten JM, Celum C, Bangsberg DR. **Periconception pre-exposure prophylaxis to prevent HIV transmission: benefits, risks, and challenges to implementation.** HIV 2010; 24:1975.

Matthews LT, Beyeza-Kashesya J, Cooke I, et al. **Consensus statement: Supporting Safer Conception and Pregnancy For Men And Women Living with and Affected by HIV.** HIV Behav 2018; 22:1713.

Melo MA, Meseguer M, Bellver J, et al. **Human immunodeficiency type-1 virus (HIV-1) infection in serodiscordant couples (SDCs) does not have an impact on embryo quality or intracytoplasmic sperm injection (ICSI) outcome.** Fertil Steril 2008; 89:141.

Mencaglia L, Falcone P, Lentini GM, et al. **ICSI for treatment of human immunodeficiency virus and hepatitis C virus-serodiscordant couples with infected male partner.**Hum Reprod 2005; 20:2242.

Meseguer M, Garrido N, Gimeno C, et al. **Comparison of polymerase chain reaction-dependent methods for determining the presence of human immunodeficiency virus and hepatitis C virus in washed sperm.** Fertil Steril 2002; 78:1199.

Moragianni VA**. Why are we still, 20 years later, depriving human immunodeficiency virus-serodiscordant couples of equal access to fertility care?** Fertil Steril 2014; 102:352.

Nicopoullos JD, Almeida PA, Ramsay JW, Gilling-Smith C. **The effect of human immunodeficiency virus on sperm parameters and the outcome of intrauterine insemination following sperm washing.** Hum Reprod 2004; 19:2289.

Ohl J, Partisani M, Wittemer C, et al. **Assisted reproduction techniques for HIV serodiscordant couples: 18 months of experience.** Hum Reprod 2003; 18:1244.

Ohl J, Partisani M, Wittemer C, et al. **Encouraging results despite complexity of multidisciplinary care of HIV-infected women using assisted reproduction techniques.** Hum Reprod 2005; 20:3136.

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of

Health and Human Services. Available at http://HIVinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf (Accessed on March 01, 2020).

Peña JE, Klein J, Thornton M 2nd, et al. **Successive pregnancies with delivery of two healthy infants in a couple who was discordant for human immunodeficiency virus infection.** Fertil Steril 2002; 78:421.

Pennings G. **The physician as an accessory in the parental project of HIV positive people.** J Med Ethics 2003; 29:321.

Phelps JY. **Restricting access of human immunodeficiency virus (HIV)seropositive patients to infertility services: a legal analysis of the rights of reproductive endocrinologists and of HIV-seropositive patients.** Fertil Steril 2007; 88:1483.

Practice Committee of American Society for Reproductive Medicine. Recommendations for reducing the risk of viral transmission during fertility treatment with the use of autologous gametes: a committee opinion. Fertil Steril 2013; 99:340.

Practice Committee of American Society for Reproductive Medicine. Hepatitis and reproduction. Fertil Steril 2008; 90:S226.

Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States. https://HIVinfo.nih.gov/contentfiles/lvguidelines/glchunk/glchunk_153.pdf (Accessed on August 07, 2015).

Safier LZ, Grossman LC, Sauer MV, Douglas NC. **Sperm washing with intrauterine insemination and preexposure prophylaxis: an innovative approach to treating HIV-serodiscordant couples.** Am J ObstetGynecol 2017; 216:617.

Santulli P, de Villardi D, Gayet V, et al. **Decreased ovarian reserve in HIV-infected women.** HIV 2016; 30:1083.

Santulli P, Gayet V, Fauque P, et al. **HIV-positive patients undertaking ART have longer infertility histories than age-matched control subjects.** Fertil Steril 2011; 95:507.

Sauer MV, Chang PL. **Establishing a clinical program for human immunodeficiency virus 1-seropositive men to father seronegative children by means of in vitro fertilization with intracytoplasmic sperm injection.** Am J ObstetGynecol 2002; 186:627.

Sauer MV, Denison R, Rankin T, Solomon S. **Roundtable discussion.** J Acquir Immune Defic Syndr 2005; 38 Suppl 1:S39.

Sauer MV, Wang JG, Douglas NC, et al. **Providing fertility care to men seropositive for human immunodeficiency virus: reviewing 10 years of experience and 420 consecutive cycles of in vitro fertilization and intracytoplasmic sperm injection.** Fertil Steril 2009; 91:2455.

Savasi V, Parisi F, Oneta M, et al. **Effects of highly active antiretroviral therapy on semen parameters of a cohort of 770 HIV-1 infected men.**PLoS One 2019; 14:e0212194.

Scavalli CP, Mandelbrot L, Berrebi A, et al. **Twin pregnancy as a risk factor for mother-to-child transmission of HIV-1: trends over 20 years.** HIV 2007; 21:993.

Semprini AE, Levi-Setti P, Bozzo M, et al. **Insemination of HIV-negative women with processed semen of HIV-positive partners.** Lancet 1992; 340:1317.

Shang G, Seed CR, Wang F, et al. **Residual risk of transfusion-transmitted viral infections in Shenzhen, China, 2001 through 2004.** Transfusion 2007; 47:529.

Stevens CE, Beasley RP, Tsui J, Lee WC. **Vertical transmission of hepatitis B antigen in Taiwan.** N Engl J Med 1975; 292:771.

Steyaert SR, Leroux-Roels GG, Dhont M. **Infections in IVF: review and guidelines.** Hum Reprod Update 2000; 6:432.

Stora C, Epelboin S, Devouche E, et al. **Women infected with human immunodeficiency virus type 1 have poorer assisted reproduction outcomes: a case-control study.** Fertil Steril 2016; 105:1193.

Stramer SL, Notari EP, Krysztof DE, Dodd RY. **Hepatitis B virus testing by minipool nucleic acid testing: does it improve blood safety?** Transfusion 2013; 53:2449.

The American with Disabilities Act. One hundred and first Congress of the United States of America, second session, Washington DC on Tuesday, the twenty-third of January, 1990.

Van Leeuwen E, Repping S, Prins JM, et al. **Assisted reproductive technologies to establish pregnancies in couples with an HIV-1-infected man.** Neth J Med 2009; 67:322.

Vankerkem P, Manigart Y, Delvigne A, et al. **In vitro fertilization when men, women, or both partners are positive for HIV: a case-control study.** Arch GynecolObstet 2017; 295:1493.

Vernazza PL, Graf I, Sonnenberg-Schwan U, et al. **Preexposure prophylaxis and timed intercourse for HIV-discordant couples willing to conceive a child.** HIV 2011; 25:2005.

Vitorino RL, GrinsztejnBG, de Andrade CA, et al. **Systematic review of the effectiveness and safety of assisted reproduction techniques in couples serodiscordant for human immunodeficiency virus where the man is positive.** Fertil Steril 2011; 95:1684.

Wasley A, Grytdal S, Gallagher K, **Centers for Disease Control and Prevention (CDC). Surveillance for acute viral hepatitis--United States, 2006.** MMWRSurveillSumm 2008; 57:1.

Williams CD, Finnerty JJ, Newberry YG, et al. **Reproduction in couples who are affected by human immunodeficiency virus: medical, ethical, and legal considerations.** Am J ObstetGynecol 2003; 189:333.

World Health Organization. Guidelines on assessing donor suitability for blood donation. http://iacld.ir/DL/elm/whoblooddonorselectionguidelinesonassessingdonorsuitabilityfor blooddonation.pdf (Accessed on December 07, 2015).

World Health Organization. Hepatitis B fact sheet. http://www.who.int/mediacentre/factsheets/fs204/en/ (Accessed on December 07, 2015).

Zafer M, Horvath H, Mmeje O, et al. **Effectiveness of semen washing to prevent human immunodeficiency virus (HIV) transmission and assist pregnancy in HIV-discordant couples: a systematic review and meta-analysis.** Fertil Steril 2016; 105:645.

Zou S, Stramer SL, Notari EP, et al. **Current incidence and residual risk of hepatitis B infection among blood donors in the United States.** Transfusion 2009; 49:1609.

Zutlevics T. **Must ART be offered to HIV-serodiscordant and HIVseroconcordant couples: an ethical discussion?**Hum Reprod 2006; 21:1956.