

Taskforce 8: Ethics of medically assisted fertility treatment for HIV positive men and women

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In this 8th statement of the ESHRE Taskforce on Ethics and Law, the focus is on the ethical issues raised by (assisted) reproduction for HIV positive men and women. Due to treatment improvements, their life expectancy has increased substantially. This, in combination with the reduction of perinatal transmission to the child, makes the creation of a family more acceptable. Recommendations are made concerning methods of avoiding HIV transmission in the couple and to their offspring. It is concluded that, if certain precautions are taken, medical assistance to reproduction of HIV positive people is ethically acceptable. For the time being, only cases of serodiscordant couples should be considered.

Introduction

A major increase in the life expectancy and life quality of HIV infected persons has resulted from treatment improvements. These changes mean that HIV + people who often avoided or were advised to avoid procreation have reconsidered their reproductive plans. Furthermore, a significant reduction in the perinatal transmission of the virus has made these plans more acceptable. Thus, an increased number of HIV + men or women are seeking advice and/or treatment in order to create their family.

Scientific background

This document addresses the problems of providing medically assisted fertility treatment for HIV + men and women in the western world where the life prospect as well as treatment options are significantly different from many developing countries.

Life expectancy

Prior to the use of Highly Active Anti-Retroviral Therapy (HAART), the average time from HIV infection to development of symptoms was 8 years and to death, 13 years. Prognosis has been shown to be related to age (worse if >50 years), CD4 + ve T-cell count, viral load and prior AIDS diagnosis. For example, a man with a viral load >5000 copies/ml and CD4 >200 cells/mm³ has a 3.7% chance of disease progression in 3 years whereas a man with viral load >55 000 copies/ml and a CD4 of <50 cells/mm³ has an 85% chance of progression to AIDS in 3 years.

For patients with access to treatment, the prognosis is now radically better but estimates of life expectancy, as in most

diseases, are not yet robust, as HAART has been widely prescribed only since 1996. The improvement in prognosis is however related to the patient's ability to adhere to complicated treatment regimens over long periods of time, and this should be considered when estimating an individual's likely survival.

Many cohorts have examined the difference in survival between men and women but the results remain conflicting, suggesting that any effect is probably not large. Women appear to have a lower viral load for any given CD4 count or time since sero-conversion, but as treatment guidelines are now based on CD4 counts, this is of no great significance in the management of patients.

Vertical transmission

An untreated mother who delivers vaginally and breastfeeds her baby has a 28% chance of infecting her baby. Transmission is associated with viral load (there is however no viral load below which transmission never occurs), CD4 count, maternal health and prematurity (increased risk with delivery before 34 weeks). With anti-retroviral therapy, Caesarean section and bottle feeding, the risk of vertical transmission is <3%. Caesarean section has been shown to decrease transmission in a cohort study and a randomized controlled trial, but these were conducted before most women were offered combination anti-retroviral therapy. With HAART it is now uncertain whether, or how much, elective Caesarean section further diminishes the transmission rate.

At present, there is no proof that ICSI might give a risk reduction as compared to insemination with washed sperm in cases of male HIV +. Both the advantages and the disadvantages are based on theoretical ideas (less exposure to

infected material versus rupture of the oocyte membrane and full entry of sperm membrane).

The effects and long term risk for the child of antiviral therapy are still under clinical investigation, but no consistent pattern of adverse outcome has yet emerged.

Effect of pregnancy on maternal health

There is little increased risk of disease progression or death caused by pregnancy itself if the mother is well at the outset.

Safety of anti-retroviral drugs during pregnancy

All anti-retroviral drugs are associated with side effects and many of these are severe. Whether the risk of serious side effects is increased, or decreased, during pregnancy is not known with certainty, but case reports of maternal deaths have led to guidance regarding didanosine and stavudine in combination.

An International Registry of Outcomes of Pregnancies exposed to anti-retrovirals has not yet identified any specific neonatal syndrome associated with exposure to any individual drug, but the numbers reported are still small. In particular, there are few data concerning exposure to anti-retroviral drugs in the first trimester. Some anti-retroviral drugs (based on animal studies) are regarded as less safe for the fetus, e.g. efavirenz.

Horizontal transmission

Estimates of the risk of transmission of HIV between heterosexual partners have shown that this is related to the presence of other sexually transmitted infections (especially ulcerative conditions), viral load and the disease stage of the infected partner. Transmission from man to woman appears more likely than from woman to man. Estimates of the risk per sexual act are imprecise. As treatment with anti-retroviral drugs lowers viral load, it is assumed that this also decreases infectivity with unprotected intercourse. However, as viral load in blood and genital secretions are not always related, this cannot be relied upon.

Risk to other patients and the therapeutic team

Ideally all labs should take universal precautions. Furthermore, as there is evidence of contamination both to samples of other patients, to other patients and to the personnel involved, it is considered good practice to have a separate laboratory and well informed and trained personnel to treat these cases.

Ethical considerations

Fundamental ethical principles

The question of treating HIV + men and women generates conflicts between two ethical principles, respect for the autonomy of the patients to decide about their reproduction, and the principle of beneficence as expressed in the concern for the welfare of the child.

Information and autonomy

Information is generally considered as the key to enhancing patients' autonomy. There is a need for good information for

the public in general, as the matter is in constant evolution: risk of transmission, progress of the disease and treatment are rapidly changing. These factors are relevant to the ethical evaluation regarding treatment of these HIV + patients. Furthermore, informing the public will also indirectly contribute to the reduction of the spread of the disease.

Responsibility

There are several dimensions of responsibility to consider. The patients have a duty to inform the team of their HIV status, so that necessary precautions can be taken by all concerned. Patients should also comply with the most effective treatment for their condition, both for their partner's and for the future child's sake. The physician has a responsibility towards the couple and their future offspring. The specific risks involved in this treatment should be fully explained, and accepted by, the patients. Nevertheless, the welfare of the child is a joint responsibility of the physicians and intentional parents.

In the case of HIV infection we have to distinguish two groups with their different needs: fertile and infertile couples.

(i) The rationale for intervention in fertile couples is avoiding harm to the uninfected spouse, and indirectly, to the future offspring. Since these couples are able to procreate by themselves, the contribution of the physician is directed at risk reduction rather than helping with conception. Risk reduction *per se* is part of the physician's obligation and is itself relevant to the ethical decision making process. This is why it is considered good practice to use insemination with washed sperm in fertile couples where the male partner is HIV +, and also to use insemination when the female partner is HIV +, in order to decrease the risk of her contaminating her partner by unprotected intercourse. When the woman is pregnant and infected, she should accept treatment with anti-retroviral agents, agree to a Caesarean section if necessary, and agree to bottle feeding.

(ii) When the couple also suffers from infertility, the goals of contributing to the conception and of reducing horizontal risk conflate. By offering treatment, the physician assumes special responsibility for the future offspring, since that particular child would not be conceived without medical intervention. To determine the acceptability of any risk, we should take into account its gravity (short and long term consequences and outlook of the disease) for the parents and offspring, and its probability for the offspring.

There is no reason to exclude these couples from the usual considerations applied to all couples seeking infertility treatment. *Per se*, the additional risk of transmitting the disease to the child linked to the HIV infection is not excessively high at present, compared to the risk accepted for older women, people with chromosomal abnormalities, or multiple pregnancies, and to the base rate risk of congenital abnormalities in the general population. This risk is considered acceptable, although it may be additive to the aforementioned risks.

The welfare of the child is not only physical, but also includes a psycho-social dimension, i.e. the risk of being

orphaned at a vulnerable age and of growing up in a family which is confronted with a serious illness. There is an agreement that, in general, the death of a parent is one of the most devastating traumas a child can experience. Nevertheless, the life expectancy of HIV + parent may be comparable to that of a parent who suffers from cancer, or from a genetic disease such as cystic fibrosis. However, it is suggested that medical assistance in ART should only be considered for the time being for sero-discordant couples so that at least one parent is likely to be able to raise the child until adulthood. This proposal may be adjusted when long term studies show that the life expectancy of the symptomatic patients with the new therapies is considerably improved.

Specific problems

Engaging in fertility treatment implies agreement to disclose the HIV status to the reproductive partner. The confidentiality regarding private medical information cannot be respected within this context.

Taking into account the risks to the future child, to the partner, the other fertility patients and to the caring team, it is recommended that all infertility patients are screened for HIV. Efforts should be made to convince patients of the benefits of knowing their HIV status. Those patients who refuse screening after full information should be treated with the same precautions as if HIV + .

In the case of specific life style risks, the physician has the right to refuse collaboration in cases which may compromise

parental competence and/or jeopardize the welfare of the child, such as non-compliance to HIV treatment, drug abuse, etc. Such conditions should be evaluated on a case by case basis.

It is recommended that HIV infected people are treated in reference centres with established protocols, especially as there are often other co-viruses which necessitate specific care for the patient (e.g. hepatitis B and C). Very careful evaluation of both the clinical part of the programme (i.e. oocyte retrieval) and of the laboratory conditions should be performed to ensure safety. A separate adapted laboratory as well as separate tanks for storage of infected material is recommended.

All new protocols should be rigorously evaluated. The centre should offer care from a multi disciplinary team including clinicians (fertility experts, HIV experts, obstetricians) biologists and embryologists. These centres should also have access to counsellors/psychologists with expertise in the care of HIV patients.

Rigorously tested large studies with follow-up of couples and their children are necessary to assess the long term safety of the methods of treatment.

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