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Prevention of perinatal HIV transmission

Frits van Griensven *

Introduction

In the last five years HIV has been spreading more rapidly among women of child-bearing age than among other population groups. This has increased the number of children born to HIV infected mothers, particularly in the developing world. WHO estimates that by 1994 more than 1.5 million children had been infected world wide, the majority in sub-Saharan Africa and the Americas. By the year 2000 this number will have increased to 4 million.¹ HIV infected children may not only be affected by their own disease, but also by the process of deterioration and death of parents and siblings and ultimately by their own orphanhood. Also they might experience fear, rejection and discrimination from the environment. What the mental and social consequences of these experiences are is difficult to say, but the immediate human suffering is considerable. The best way to prevent HIV infection in children is prevention of HIV infection in women, but for a number of reasons this cannot always be achieved. In these cases voluntary avoidance of pregnancy, abortion and prevention of transmission from mother to child are the only preventive possibilities. Legal sanctions against pregnancy or mandatory abortion

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¹ Stoneburger RL, Sato P, Burton A, Mertens T. The global HIV pandemic. *Acta Paediatr* 1994; suppl 400: 1-4.

and treatment are not acceptable as they are considered against the Universal Declaration of Human Rights of 1948. In a recent statement of the Joint United Nations Programme on HIV/AIDS (UNAIDS) it is said that it is the "right of all women and men..... to determine the course of their reproductive life and health" and "where the welfare of children is concerned that decisions are made in keeping with children's interests."² Thus, parents have the right to decide whether they want to have children but they should weigh this right against the likelihood that they will impose human suffering on their children through HIV infection. However, in medical practice the decision of parents to have children will depend heavily on the actual probability of HIV transmission to the offspring and on the attitudes and advice of antenatal health care professionals and underlying policies. Since the beginning of the HIV epidemic our knowledge regarding prevention of transmission from mother to child has increased considerably and several interventions have shown to substantially decrease the risk of transmission. In this paper we will review the development in knowledge and the ensuing changes in attitudes and practice regarding perinatal HIV transmission in the Western and developing world. Finally we will identify areas where more research is urgently needed.

Transmission of HIV to the child

The risk of HIV transmission from mother to child has been evaluated in a number of studies, generating estimates varying from 13% to 32% in Western countries and from 25% to 42% in the developing world.³ The higher risk in developing countries has been contributed to the practice of breast feeding which is necessary for the survival of

² Anonymous. HIV and infant feeding. *W Epidemiol Rec* 1996; 39: 289-91.

³ Dabis F, Msellati P, Dunn D. Estimating the risk of mother to child transmission of HIV; Report of a workshop on methodological issues, Ghent, Belgium. *AIDS* 1993; 7: 1139-48.

children.⁴ In Thailand the risk of mother to child transmission of HIV appears to be equal to estimates from the Western world despite suggestions of higher infectivity of HIV subtype-E which circulating here.⁵ Actual infection of the child can occur before, during and after birth, knowledge of which is essential for the implementation of preventive measures. In-utero and intrapartum transmission have been well documented and it is estimated that 35% of infections occur during pregnancy and 65% in the final six weeks of gestation and during delivery.⁶ When a newborn is not infected at birth an additional 14% risk of infection results from breast-feeding. The exact mechanism of transmission is not known but it has been suggested that cell to cell placental transmission may be responsible for infection in utero, whereas exposure to maternal blood and secretions during delivery is likely to cause infection intrapartum. Ingestion and mucosal exposure to infected cells during breastfeeding incites postpartum infection. Maternal risk factors for transmission are the stage of disease in the mother and marker cells of disease progression such as low levels of T helper cells, increased levels of circulating virus etc.

Prevention of transmission

HIV testing

HIV screening programs for women of childbearing age and pregnant women may help identify those at risk for HIV infection and those already infected. The first

⁴ Reggy A, Simonds RJ, Rogers M. Preventing perinatal HIV transmission. *AIDS* 1997 (in press).

⁵ Shaffer N, Bhiraleus P, Chinayon P. et al. High viral load predicts perinatal HIV-1 subtype E. transmission, Bangkok, Thailand. Xth International Conference on AIDS, Vancouver Canada, July 1996 [abstract Tu C343].

⁶ Rouzioux C, Costaglioloa D, Burgard M, et al. Timing of mother to child transmission depends on maternal status. *AIDS* 1993; 7: S49-52.

group can be educated to avoid risk behavior (unprotected sex, use of unsterile injecting equipment) in order to avoid infection, the second group can be informed about the risk of transmission to the offspring and about possible intervention methods. In many countries around the world such screening programs have been implemented and there has been a heated debate among health care professionals whether these programs should be voluntary or mandatory. Mandatory screening may discourage women to seek prenatal care which may actually lead to an increase in the number of newborns infected with HIV. This may particularly be the case for those at the highest risk for HIV infection. On the other hand, mandatory programs may pick up infections that would have gone unnoticed otherwise because people do not consider themselves at risk. Recently the American Medical Association approved a resolution calling for mandatory screening of pregnant women and newborns, but specialty organisations such as the American College of Obstetricians and Gynecologists and the American Academy of Pediatrics fiercely oppose the idea. A statement issued by the organisations said that "pregnant women receive HIV education and counselling and that testing be recommended but emphasized that the decision should be an "educated judgement" by a "fully informed" patient."⁷ However, informing pregnant women about their HIV positive status has shown to be effective in decreasing the number of pregnancies. In the European study among HIV positive women for instance it appeared that pregnancy rates decreased by more than fifty percent after women were informed of their HIV positive status.⁸

⁷ Rovner J. US specialists object to AMA's call for mandatory HIV testing. *Lancet*, 1996; 348: 330.

⁸ European Working Group on the Natural History of HIV infection in Women. Incidence of pregnancy in a European cohort of HIV infected women. Paris, WHO European Collaborating Centre on HIV/AIDS, 1996.

Abortion

In the earlier days of the epidemic HIV infected women were advised to avoid pregnancy, and if pregnant it was recommended to undergo an abortion. In 1986 and 1990 the Health Council of the Netherlands for instance published official guidelines in which these policies were formulated. It was thought that pregnancy would accelerate disease progression in the mother and the probability of transmission from mother to child was estimated to be over 50 percent at that time.⁹ However these conclusions were based upon retrospective studies in which mothers were traced from children who had developed AIDS. In more recent prospective studies it appeared that a mother in more advanced stages of HIV infection was more likely to transmit the virus to her offspring which in turn had a more rapid progression of the disease. The abortion policy was widely followed in the Netherlands and other European countries, and approximately 70 percent of pregnancies in HIV infected women were terminated. However, in many cases abortion did not end the wish of women to have children and as a result secondary pregnancies occurred but now in later stages of infection, increasing the risk of transmission and a more severe course of disease in the child.

Antiretroviral drugs and other interventions

In recent years large progress has been made in the prevention of perinatal transmission through the use of antiretroviral drugs. In a placebo-controlled study of the efficacy of Zidovudine (ZDV or AZT) to decrease mother child transmission it was shown that this drug was safe and effective in reducing vertical transmission from 25 to 8 percent.¹⁰

⁹ Scott GB, Fischl MA, Klimas N, et al. Mothers of infants with the acquired immunodeficiency syndrome. Evidence for both symptomatic and asymptomatic carriers. *JAMA*, 1985; 253: 363-6.

¹⁰ Centers for Disease Control. Zidovudine for the prevention of HIV transmission from mother to child. *Morbidity and Mortality Weekly Report* 1994; 43: 285-7.

ZDV was given to women with more than 200 CD4 cells five times per day in 100 mg doses orally starting between 14 and 34 weeks of gestation, intravenously during labor and delivery and to the neonate four times daily for six weeks within 24 hours after birth. The result of this study has changed the policies and recommendations for pregnant women and women of childbearing age worldwide. Prenatal treatment with ZDV of HIV infected women is now standard in the Western world and strongly recommended elsewhere. However, the complexity and costs of the ZDV regimen as described above indicates that it is largely impractical and inaffordable in developing countries. Health care facilities need to have high standards for laboratory testing and monitoring and treatment costs can be as high as 1500 US\$ per mother-child pair. Cesarean section is another method to prevent HIV transmission which is studied by a number of groups. Results point in the same direction but are variable with a reduction of transmission varying between 20 and 50 percent.¹¹ From these data it can be calculated that between 12 and 16 sections are needed to prevent one case of perinatal HIV transmission.¹² Because these surgical interventions are quite expensive and require a high level of care they are not practical in large parts of the world. And if they are applicable their use is far outweighed by the benefits and prospects of ZDV treatment. A second obstetrical method which has been studied to prevent transmission is vaginal washing with chlorhexidine to disinfect the birth canal prior to delivery. A study performed in Malawi however showed that this method was no more effective in preventing vertical transmission than was no intervention at all. Since vaginal washing is an easy procedure it is worthwhile to explore this avenue further with other liquids and microbicidal agents in varying concentrations.

It has also been suggested that passive immunization of mother-child pairs with neutralizing antibodies collected from HIV seropositive individuals may be effective in

¹¹ Bryson YJ. Perinatal HIV-1 transmission: recent advances and therapeutic interventions. *AIDS* 1996; 10 (suppl 3): S33-S42.

¹² Scarlatti G. Paediatric HIV infection. *Lancet* 1996; 348: 863-8.

reducing mother to child transmission. This method would work similarly to the one used to provide protection against primary hepatitis A and B infection by passively immunizing individuals with hepatitis immunoglobuline. Phase I and II studies exploring the safety and efficacy of HIV immunoglobulin are underway but results are not yet available.

A simple strategy to prevent a number of mother to child transmissions in developing countries is a change from breast-feeding to bottle-feeding. However as long as the risk of HIV transmission through breast-feeding outweighs the risk of dying through other childhood diseases and malnutrition it will be difficult to change this practice. To study the risk of breast-feeding versus bottle-feeding for HIV infection and death more in detail recently a study has started in Nairobi, Kenya. Hopefully results of this study will provide more insight in the risks of breast-feeding compared to bottle-feeding and will help developing programs that are easily applicable in developing countries.

Conclusion

Recently large progress has been made in reducing perinatal HIV transmission rates from 25 to 8 percent through antiretroviral treatment. This achievement has completely changed the picture of prevention of mother to child transmission in the Western world but not so in developing countries where these treatments are not affordable and not practical. Whereas in the developed world the success of antiretroviral treatment is likely to overshadow the classic means of preventing HIV transmission such as avoidance of pregnancy and abortion, in developing countries these are still the two first strategies to be applied. More progress in the area of antiretroviral treatment is to be expected as promising new combinations of drugs are now being tested and results are underway. No satisfactory alternative is yet available to prevent perinatal HIV transmission in the developing world. Bottle-feeding versus breast-feeding is being studied and other methods such as vaginal cleansing prior to delivery have shown to be ineffective. Therefore studies investigating the protective effect of the use of disinfectants and microbicidal agents prior

and during delivery in varying concentrations are urgently needed. Passive HIV immunization of mother-child pairs might be another interesting option for the developing world but safety and efficacy of this method still needs to be shown.

In the previous years many parents who have inhibited their wish to have children may now feel that the risk is becoming acceptable. A chance of 1:12.5 of giving birth to an HIV infected child is one that many are willing to take. As a result, the positive effect of antiretroviral therapy on perinatal transmission may be partially eliminated because more HIV infected mothers may decide to have children. Although this observation may sound negative, it should be seen as an indication of the prosperity of the Western world compared to developing countries, where effects like this are still far away. Therefore more attention should be given to the development of simple and affordable methods which can prevent mother to child transmission in developing countries to the same rate as is currently possible in the West.