Nigerian Journal of Paediatrics 2002; **29** (**3**): 55-60

REVIEW ARTICLE

Towards reducing Mother-to-Child Transmission of HIV

I Emodi*

Summary

Emodi I. Towards reducing Mother-to-Child Transmission of HIV. *Nigerian Journal of Paediatrics* **2002; 29: 55.** Women of child bearing age in Africa are particularly vulnerable to HIV infection, and this has led to an increase in the number of paediatric HIV infections reported due to mother-to-child transmission (MTCT) of HIV during pregnancy, delivery and breastfeeding. Various approaches to prevent or reduce MTCT have been established. These include elective Caesarean section delivery, avoidance of breastfeeding and antiretroviral therapy. For these strategies to be put in place, effective voluntary and confidential HIV counseling and testing for pregnant women should be implemented in African countries. Prevention of MTCT should also be considered as part of the wider management of maternal and infant health during prenatal, delivery and postnatal care. This review attempts to bring into focus the various strategies for a reduction in MTCT with special emphasis on the problems encountered in Africa.

Key Words: HIV, Reducing perinatal transmission

Introduction

MOTHER-TO-CHILD transmission (MTCT) is the overwhelming source of Human Immunodeficiency Virus (HIV) infection in young children and virtually the only source in countries where blood products are regularly screened and clean syringes and needles are widely available.[1] In 1999, an estimated 570,000 children aged 14 years or younger became infected with the HIV virus. Of these, almost 90 percent were in sub-Saharan Africa due to a combination of high HIV prevalence in pregnant women and a high fertility rate.[2] The virus may be transmitted during pregnancy, labour, delivery, or after the child is born during breastfeeding.[3,4] Each method of transmission has its own mechanism, risk factors, and interventions. Most studies suggest that the probability that an HIV-positive woman's baby will have the virus ranges from 15 to 25 percent in an industrialized country if there is no treatment with anti-retroviral drugs, and 25 to 45 percent in a developing country.[1,3] The frequency and duration of breastfeeding, maternal characteristics and factors surrounding the delivery can explain these differences.

Factors which facilitate transmission include low levels of CD4 cell count (less than 4400/mm^3), high viral load,[5,6] vitamin A deficiency,[7] late stage of immunosuppression i.e. AIDS p24-antigenaemia, prematurity, and chorioamnionitis due to sexually transmitted diseases.[8] Instrumentation[9] such as forceps delivery, episiotomy, fetal scalp monitors, and vacuum extraction also facilitate virus transmission. Rupture of membranes for longer than four hours has also been proved to increase the chances of transmission.[10] Transmission rates can be decreased by giving antiretroviral drugs to mother and child,[11] and by approximately 50 percent with elective Caesarean section as compared with other modes of delivery.[12] Omission of breastfeeding also decreases the rate of transmission.[13] Usually a combination of the above is necessary for the best result.[14-16] In the United States of America, MTCT of less than two percent has been achieved with elective Caesarean section, antiretroviral drug therapy and omission of breastfeeding.[3]

Voluntary Counseling and Testing

As interventions become more widespread, HIV-infected women will have to know their HIV status

University of Nigeria Teaching Hospital, Enugu

Department of Paediatrics
*Senior Lecturer

in order to benefit from them. This means testing with the informed consent of the woman, using reliable test kits and ensuring complete confidentiality. Voluntary counseling and testing (VCT) will therefore be required on a larger scale than is currently available in most countries. Women who know that they are HIV infected can make informed decisions about childbearing and infant feeding. In the United Kingdom, voluntary HIV testing began in 1987 with an uptake of 17 percent.[17] By August 1999, the British government had initiated a policy whereby VCT was made a routine and integral part of antenatal care across England; Wales and Scotland were to follow suit.[18] In the USA, the findings of the Perinatal AIDS Clinical Trials Group Protocol 076[11] were incorporated into the health care system in 1995.[3] Obstetric standards and published guidelines strongly recommend HIV testing and elective Caesarean section to all pregnant women. In some states, this is mandatory.[19]

Cartoux *et al*[20] found in several African countries, that VCT is feasible and acceptable for pregnant women. They obtained a median acceptability of 69 percent, with a range of 33-95 percent, but found that the return-rate for test results affected the overall acceptability.

In an earlier report, they also noted that those tested during their last trimester were unlikely to return for the test results.[21] This problem of women not returning for their test results might be solved with the use of point-of-care HIV screening tests which does not require laboratory facilities, is user friendly and yields a result within 30 minutes. Taking local conditions into account therefore, policy-makers need to decide what kind of counseling and testing services are most appropriate and feasible, and what action, if any, is required to strengthen the health system that supports them.

Antiretroviral Therapy

In 1994, Conners *et al* [11]reported the findings of the AIDS Clinical Trials Group (ACTG) Protocol 076 and opened the door to a major effort to reduce perinatal infection with HIV. They reported a decline of 66 percent in the transmission rate with a regimen of zidovudine, a nucleoside reverse transcriptase inhibitor, given ante-partum orally from 14 to 34 weeks, intravenously during labour to the mother and to the newborn for six weeks in pregnant women with mildly symptomatic HIV diseases. The mother did not breastfeed. In Europe and the United States, zidovudine prophylaxis has been largely superceded by prophylaxis with a combination of antiretroviral agents.[22] The high cost of these regimens, absence of VCT services, and lack of antenatal care make it impracticable for women in developing countries. Other factors include late registration at antenatal clinics, deliveries attended by unskilled personnel, a large percentage of home deliveries, and lack of safe affordable breast milk substitutes. Subsequently, results of randomized clinical trials conducted in the developing world indicated that shorter antenatal regimens, that begin as late as the time of delivery, and perhaps given only to the newborn, are effective in reducing the risk of perinatal transmission.[23-25] The study in Kampala, Uganda, showed that the drug nevirapine, a non-nucleoside reverse transcriptase inhibitor, is effective when given orally to the mother during labour and only once to the baby within 72 hours of delivery.[23] The babies were still breastfed. Here, the risk of transmission was 13 percent compared to 25 percent when zidovudine was used. The low cost of the drug ($4 per dose) and the ease of administration make it extremely attractive to health workers in developing countries. The researchers concluded by suggesting that if the drug proves safe in the long term, it should be offered before or at the onset of labour to all pregnant women in areas of high HIV prevalence without testing for HIV infection. The World Health Organization has urged caution.[26]

Problems envisaged with these therapies include emergence of resistant strains and drug toxicity. Zidovudine has been proved to be relatively safe to both babies and mothers, a mild and reversible anaemia being the major immediate toxic event.[27] Of concern is the report of a small number of patients with mitochondrial dysfunction after exposure to antiretroviral therapy.[19] Given the fatal nature of HIV, any long term risk entailed by the *in utero* or neonatal exposure of children to antiretroviral drugs would have to be profound, occur early in life, and occur in a substantial proportion of those exposed, in order to outweigh the proven benefit of antiretroviral prophylaxis in reducing perinatal transmission of HIV.

Replacement Feeding

It has been established beyond doubt that HIV can be transmitted through breastfeeding.[12] The risk is between 12 and 14 percent but rises to 25 percent when the mother seroconverts after delivery.[3, 12] Physical factors such as cracked nipples and mastitis in the mother and oral thrush in the infant are potentially important risk factors for breastmilk transmission of HIV. Other risk factors include trauma to the oral mucosa by vigorous suction or loss

of mucous membrane integrity from vitamins A and B deficiency and high viral load of the mother.[28] In countries like Europe and America, counseling of HIV-positive women include the use of a safe alternative to breastmilk. Unfortunately, majority of women who risk transmitting the virus come from cultures where breastfeeding is the norm and replacement feeding presents great difficulties. Reducing the length of breastfeeding also results in a decreased risk,[24,29] but this will most likely be affected by maternal viral load[13] and vitamin A level.[30] The use of breast milk substitutes could place infants at risk of death from diarrhoeal diseases and acute respiratory tract infections related to unsafe water supply and loss of immunological protection afforded by breast milk. It may place a substantial social stigma on these mothers, which may jeopardize survival outcomes for women and their offspring because of violence and abandonment. It is also of comparable expense to other perinatal intervention strategies. In the early 1990s, women from areas where infectious diseases are a common cause of death in childhood were still advised by WHO to breastfeed their children despite the risk.[31] This policy has now been changed by a joint WHO, UNAIDS and UNICEF guideline and HIV-positive women in these areas are counseled on the risks involved in breastfeeding their baby and allowed to make the decision themselves.[32]

Elective Caesarean Section

Since a substantial proportion of MTCT of HIV-1 is thought to occur during the intrapartum period, elective Caesarean section would reduce vertical transmission of HIV because of minimal contact with infected secretions and blood in the birth canal and avoidance of contact with maternal blood from episiotomy and instrumental procedures. Other reasons include reduction of risk of ascending infection with an intact membrane, a shortened gestation period during which time maternal-fetal transfusions could have occurred as well as avoidance of microtransfusion of blood from mother to child during labour. The benefit of elective Caesarean section with regard to MTCT of HIV-1, must be weighed against the possible deleterious effects of surgical delivery as reports have indicated that HIV-1 positive women have an increased risk of peripartum and postpartum infections; complications that are related to their level of immunological deficiency.[12] A meta-analysis of 15 prospective cohort studies by The International Perinatal HIV Group revealed that the likelihood of vertical transmission of HIV-1 was decreased by approximately 50 per cent with elective Caesarean section, as compared with other modes of delivery independent of the effects of treatment with zidovudine.[12] Some studies have reported an additive effect of zidovudine and elective Caesarean section, with transmission rates reduced to as low as two percent.[3] In African countries, operative deliveries are not readily available, and do result in increased morbidity and have been found to be cost-effective only in countries where uptake of zidovudine is high.[3] The potential risks associated with elective Cesarean section would appear to outweigh the potential benefit in terms of decreased vertical transmission of HIV.

Prevention of Female Infection

More than 80 percent of all women are infected heterosexually and the prevalence of HIV is higher among females than among males. Reports reveal that by 1999, 12 to 13 African women were infected for every 10 African men.[2] For the younger age bracket (15-24 years), the risk for African girls is even more disproportionate. In countries where youngsters account for 60 percent of all new infections, young women outnumber their male peers by a ratio of 2 to 1.[33] Reasons for this include the fact that females are more susceptible physiologically to the agent responsible for AIDS. Men are eight times more likely to transmit HIV to a female partner through repeated, unprotected sexual intercourse than women are to men.[34,35]

For millions of women, factors that lower infection rates like abstinence, prompt care for STDs and fidelity or safe sex by condom use are irrelevant or inapplicable. This is because most women lack economic resources of their own, and fearing abandonment or violence, have little control over how and when they have sex and hence, over their risk of contacting HIV. A woman in a stable relationship who is economically dependent on her partner cannot afford to jeopardize his support even when she suspects he has HIV. Indeed, for girls and women in many cultures, sex is the "currency" in which they are expected to pay for life's opportunities.

The different roles that men and women play in a specific society and the rights and responsibilities associated with these roles is a powerful force in the HIV/AID epidemic. Men's risk of HIV infection generally comes from the number of partners they have, while women's risk comes from their partner's sexual behaviour except for commercial sex workers. The HIV epidemic has put men's sexual behaviour in the spotlight. Men are often viewed as unable to control their sexual behaviour, and are excused for not behaving responsibly. This behaviour puts women

at risk as men transmit HIV to women more efficiently than *vice versa*. In Africa, prevailing gender roles have relegated women and girls to a subordinate status, which also limits their ability to protect themselves against the HIV. In the USA, Campbell[36] noted that the heterosexual AIDS epidemic for women continues unabated because of the lack of attention to the behaviour of male sex partners. He stated that traditional gender roles need to be examined and that control of the epidemic will require a focus on men as individuals responsible for their own health and that of women. Male condoms are the primary prevention technology available to protect against HIV transmission during sexual intercourse,[35] but there are many gender-related barriers that limit their use especially as regards women.[33] The lack of a woman-controlled method to prevent sexual transmission of HIV also contributes to their increased susceptibility to HIV infection.[33]

Other Strategies

Topical application of a disinfectant or lavage of the birth canal with an antiseptic to reduce HIV transmission is an attractive procedure, which should be easy to administer and cost effective. In addition to their simplicity, the microbicides approach would avoid the HIV genetic variability problem, which complicates retroviral therapy and vaccine development. Cleansing of the vagina with chlorhexidine, a bactericidal soap, during labour has been proposed as a cheap way of reducing the baby's exposure in the birth canal but this has not been proved useful.[3] Improvement of the woman's nutritional status especially in respect of vitamin A level has been proposed as another way of reducing transmission.[30,37]

Sexually transmitted infections could possibly cause pathological insults to the placental foetal unit and therefore facilitate vertical transmission of HIV. Prompt treatment of any infection would reduce vertical transmission of HIV. Unfortunately, most women with STDs are asymptomatic and so cannot avail themselves of this strategy. Augmentation of the maternal and fetal immune response by active and passive immunization with vaccine or HIV-specific neutralizing antibodies has been proposed.[37] The development of an effective HIV vaccine is both a pressing and formidable problem. The most encouraging results to date have been achieved using live attenuated immunodeficiency virus in monkey models.[38] However, the frequency of pathogenic breakthroughs have been a deterrent to these developments.[38] A vaccine that has reached phase II field trials is AIDSVAX, a bivalent vaccine composed of gp 120 proteins found in the outer envelope of two strains of HIV. The version of the vaccine being tested in Thailand is designed to induce antibodies to HIV-1 subtype B & E. Early reports indicate that the vaccine is safe and capable of inducing antibodies.[39]

Conclusion

Prevention of pregnancy in HIV infected women is an objective that should be approached with great sensitivity. It should be approached through education and not by coercion. Reduction of MTCT to less than two percent has been reported with the use of antiretroviral drugs by the pregnant woman and the baby as well as avoidance of breastfeeding and delivery by elective Caesarean section in Europe and the United States.[3] This is possible in Africa and other developing countries if those involved in policy-making effect the necessary changes in health-care policies. Strategies for decreasing the prevalence of HIV in young girls should be intensified. This can be achieved by education of youngsters and safer sexual behaviour by all. Also, social change is needed in cultures that tolerate men's sexual promiscuity and condone unhealthy gender norms. Gender lies at the heart of social organization and distribution of power between men and women, and calls for changes in gender roles and hence behaviour, often touches emotional and political nerves. Some people view such changes as threatening while others see them as a part of the global trend towards equality and justice. The decrease in the cost of the antiretroviral drugs will help make these drugs affordable to the masses.

Acknowledgements

I wish to acknowledge the help of Professor JC Azubuike in reviewing this document and that of Mrs N Nzegwu for supplying some of the reference materials.

References

1. Lindegren ML, Steinberg S, Byers RH. Epidemiology of HIV/AIDS in children. *Ped Clin N Am* 2000; **47**: 1-20.
2. UNAIDS Joint United Nations Programme on HIV/AIDS Epidemic Update: Dec 1999.
3. Fowler MG, Simonds RJ, Roongpisuthipong A. Update of perinatal HIV transmission. *Ped Clin N Am* 2000; **47**: 21-38.
4. Borkowsky W, Wilfert CM. Acquired immunodeficiency syndrome. In: Infectious Diseases of Children. Krugman S, Katz SL, Gerson AA, Wilfert CM, eds.

St Louis Missouri: Mosby Year Book, 1992: 1-21.

5. Fang G, Burger H, Grimson R, *et al.* Maternal plasma human immunodeficiency virus type 1 RNA level: a determinant and projected threshold for mother-to-child transmission. *Proc Natl Acad Sci USA* 1995; **92**: 1210-4.
6. Khouri YF, McIntosh K, Cavacini L, *et al.* Vertical transmission of HIV-1. Correlation with maternal viral load and plasma levels of CD4 binding site anti-gp 120 antibiodies. *J Clin Invest* 1995; **95**: 732-7.
7. Sember RD, Miotti PG, Chiphangwi JD, *et al.* Maternal vitamin A deficiency and mother-to-infant transmission of HIV-1. *Lancet* 1994; **343**: 1593-7.
8. European Collaborative Study. Risk factors for mother-to-child transmission of HIV-1. *Lancet* 1992; **339**: 1007-12.
9. Coll O, Hernandez M, Boucher CA, *et al.* Vertical HIV-1 transmission correlates with high maternal viral load at delivery. *J Acquir Immune Defic Syndr Hum Retroviral* 1997; **14**: 26-30.
10. Minkoff H, Burns DN, Landesman S, *et al.* The relationship of the duration of ruptured membranes to vertical transmission of human immunodeficiency virus. *Am J Obstet Gynecol* 1995; **173**: 585-9.
11. Conners EM, Sperling RS, Gelber R, *et al.* Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Paediatric AIDS Clinical Trial Group Protocol 076 Study Group. *N Eng J Med* 1994; **331**: 1173-80.
12. Dunn DT, Newell MI, Ades AF, Peckham CA. Risk of human immunodeficiency virus type 1 transmission through breast feeding. *Lancet* 1992; **340**:585-8.
13. The International Perinatal HIV Group. The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type 1. *N Eng J Med* 1995; **340**: 977-87.
14. Dunn DT, Tess BH, Rodrigues LC, *et al.* Mother-to-child transmission of HIV: implication of variation in maternal infectivity. *AIDS* 1998; **12**: 1381-8.
15. Newell ML. Vertical transmission of HIV-1: risks and prevention. *J Hosp Infect* 1995; **30**: 191-6.
16. Taha ET. Intrapartum issues in perinatal transmission of HIV: Implications for interventions. Narsesa Monograph 1996; **5**: 15-28.
17. MeadowsJ, Chester T, Catalan J. Screening for HIV in pregnancy. *BMJ* 1994; **308**: 414-5.
18. Nicoll A, Peckham C. Reducing vertical transmission of HIV in the UK. *BMJ* 1999; **319**: 1211-2.
19. Fiore S, Newell ML. Preventing perinatal transmission of HIV-1 infection. *Hosp Med* 2000; **61**: 315-8.
20. Cartoux M, Meda N, Van-de-Perre P, *et al* and Ghent International Working Group on Mother-to-Child-Transmission of HIV. Acceptability of voluntary HIV testing by pregnant women in developing countries: an international survey. *AIDS* 1998; **12**: 2489-93.
21. Cartoux M, Msellati P, Meda N, *et al.* Attitude of pregnant women towards HIV testing in Abidjan, Cote d'Ivoire and Bobo-Dioulasso, Burkina Faso. DITRAME Stidu Group (ANRS 049 Clinical Trial). *AIDS* 1998; **12**: 2337-44.
22. Lorenzi P, Spicher VM, Laubereau B, *et al.* Antiretroviral therapies in pregnancy: maternal, fetal, and neonatal effects. Swiss Neonatal HIV Cohort Study, the Swiss Collaborative HIV and Pregnancy Study, and the Swiss Neonatal HIV Study. *AIDS* 1998; **12**: 2495-7.
23. Lallemant M, Jourdain G, Le Coeur S, *et al.* A trial of shortened zidovudine regimens to prevent mother-to-child transmission of Human Immunodeficiency Virus Type 1. *N Eng J Med* 2000; **343**: 982-91.
24. Guay LA, Musoke P, Fleming T, *et al.* Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVNET012 randomised trial. *Lancet* 1999; **354**: 795-802.
25. Witkor SZ, Ekpini E, Karon JM, *et al.* Short-course oral zidovudine for prevention of mother-to-child transmission of HIV-1 in Abidjan, Cote d'Ivoire: a randomized trial. *Lancet* 1999; **353**: 781-5.
26. Hankins C. Preventing mother-to-child tansmission in developing countries: Recent developments and ethical implications. In: Berer M, ed. Reproductive Health Matters. Oxford: Blackwell Science, 2000: 87-92.
27. Sperling RS, Shapiro DE, McShery GD, *et al.* Safety of the maternal-infant zidovudine regimen utilized in pediatric AIDS: Clinical Trial Group 076 Study. *AIDS* 1998; **12**: 1805-13.
28. Nduati R. Breast milk transmission of HIV: Implications for interventions: A review. In: Oriedi S, ed. Mother-to-child Transmission of HIV and Paediatric AIDS: Experiences from East and Southern Africa. NARESA MONOGRAPH 1994; **5**: 29-36.
29. Nagelkerke NJ, Moses S, Embree JE, Jeniskens F, Plummer FA. The duration of breastfeeding by HIV-1 infected mothers in developing countries: balancing benefits and risks. *J Acquir Immune Defic Syndro Hum Retrovirol* 1995; **8**: 176-81.
30. Fawzi WW, Hunter DJ. Vitamins in HIV disease progression and vertical transmission. *Epidemiology* 1998; **9**: 457-66.
31. UNAIDS point of view. Women and AIDS. October 1997.
32. WHO. Concensus statement from the WHO/UNICEF consultation on HIV transmission and breastfeeding. *Wkly Epid Recd* 1992; **67**: 177-9.
33. WHO UNAIDS/UNICEF. HIV and infant feeding. A guide for health care managers and supervisors. WHO, Geneva, 1998.
34. Padian NS, Shiboski SC, Glass SO, Vittinghoff E. Heterosexual transmission of human immunodeficiency virus (HIV) in northern

California. Results from a ten-year study. *Am J Epidemiol* 1997; 146: 350-7.

35. UNAIDS Technical update. Gender and HIV/AIDS. June, 1998.
36. Campbell CA. Male gender roles and sexuality: implication for women's AIDS risk and prevention. *Soc Sci Med* 1995; 41: 197-210.
37. UNAIDS Technical update. Mother-to-child transmission of HIV. November, 1997.
38. Berkhout B, Verhoef K, van Wamel JL, Back NK. Genetic instability of live, attenuated human immunodeficiency virus type 1 vaccine strains. *J Virol* 1999; 73: 1138-45.
39. CDC UPDATE Testing a Vaccine Designed to Help Curb the Devastating Toll of HIV in the Developing World. *CDC Supports Thai Health Officials and Vax Gen in Collaborative Effort. www.cdc.gov/hiv/pubs/facts/htm.*February 1999.