Anti-Retroviral Regimens for the Prevention of Mother-to-Child HIV-1 Transmission: the Programmatic Implications


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Introduction

Mother-to-Child transmission (MTCT) of HIV-1 is a major component of the AIDS epidemic, especially in sub-Saharan Africa and the less-developed countries of South East Asia. In more developed countries, obstetric interventions, anti-retroviral treatment and replacement feeding for the infant have resulted in significant reduction in transmission rates but this is not the case in the less-developed countries.2 Limited access to the above-mentioned interventions are the main reasons for the differences in transmission rates. However the prevalence of infant HIV infection will not be reduced in less developed countries unless the prevalence of HIV infection in women of reproductive age is reduced, and antenatal testing for HIV is widely available and accepted. The introduction of ARV regimens needs to be seen in this wider context. The introduction of ARV treatment will have an impact on other reproductive health programmes being carried out by developing countries. There are ethical and technical implications which will have to be addressed by policymakers and health practitioners. This paper will discuss first the general programmatic considerations, then secondly the feasibility and logistics of the different ARV regimens.

General Considerations

Mother vs Infant or Mother and Infant

Ideally MTCT prevention using ARV regimens in pregnancy or postnataally should prevent infant infection by HIV and also prolong the life of the mother. In developed countries, HIV-positive women continue after delivery with the ARV treatment they were taking before pregnancy. However in the developing countries, most women are not on any such treatment before pregnancy and current ARV regimens for MTCT prevention do not offer any continued treatment for the mother beyond the immediate postnatal period. In settings where continued ARV treatment is not affordable, women may feel that the regimens are solely or mainly for the benefit of their babies, and not for
themselves. This perception has now been voiced by women in the Zimbabwean press. Naturally, when an infant has been spared HIV prevention, the mother's attention will turn to how long she herself can remain healthy enough to look after him/her. A situation in which the ARV regimens succeed in reducing MTCT without follow up treatment of the mothers or parents could create more orphans many years from now than at present. Therefore MTCT prevention with ARV regimens should not be an end in itself but be part of a broad programme in which the other interventions for the welfare of the family are strengthened. It could also serve as an entry point which introduces the mother or parents to behavioural change, safe sex, good nutrition etc. if drug treatment is not an affordable option. These aspects should be given due weight in the MTCT prevention programmes.

**Prevention of infection in reproductive age women**

Most sub-Saharan countries have introduced mass media campaigns to inform the public about the risk of contracting HIV infection. Prevalence rates among women of reproductive age in these countries however remain high. This will mean that the magnitude of the paediatric AIDS problem will only be partly reduced by the success of ARV regimens. Reducing the number of women who are HIV positive before they become pregnant remains a priority which many countries have not tackled successfully. In recent years, voluntary HIV testing programmes have been introduced in these countries with varying degrees of success. The impact of behavioural change and voluntary testing campaigns also depends on the wide availability of condoms and contraceptive methods. In most sub-Saharan African countries where these campaigns have been introduced, condoms are not easily accessible even in the major cities. In a major city such as Harare, there are no condom vending machines at the bus or railway stations, in public toilets or any of the major hotels. Condoms are only available in pharmacies, clinics and shops. After 8 pm in Harare, a city of over 1 million people, there are only two pharmacies in the city centre which are open to sell condoms. In rural Zimbabwe, condoms are only available at primary care clinics, if they have them in stock. The female condom is even harder to obtain, and more expensive. In such a scenario, the introduction of ARV regimens may be difficult to justify.

**Antenatal HIV Testing**

The antenatal period offers a window of opportunity for voluntary counselling and testing. In sub-Saharan Africa, about 63% of women have at least one antenatal visit, although countries such as Zimbabwe and South Africa have attendance figures of over 90% 9,10,11. Even with delayed antenatal booking, ARV treatment could still be offered if rapid HIV testing was widely available and cheap. All the ARV regimens being considered for sub-Saharan African countries begin from 36 weeks or in labour. In theory then, most pregnant women would be eligible for ARV treatment, if their HIV status was known.

However, the majority of women attending antenatal care in sub-Saharan Africa do not know their HIV status. There is very little data in these countries on the proportion of
HIV positive pregnant women who know their status and are therefore eligible for ARV treatment. Voluntary testing for HIV in pregnancy has been introduced in a number of sub-Saharan African countries with modest success 18-20. To make ARV treatment worthwhile, such counselling and testing programmes will have to be sustained and even expanded in the face of much cultural resistance.

**Termination of Pregnancy**

In early pregnancy, HIV positive women should be offered termination of pregnancy. Restrictive laws on termination of pregnancy apply in most countries of sub-Saharan Africa except in the Republic of South Africa and Ghana21. In the rest of the other countries, the strict wording of the laws means that HIV infection is not a valid indication for termination of pregnancy. Women in these countries obtain permission for termination of pregnancy through a bending of the rules by health practitioners and Ministry of Health officials. Up to now the legal authorities have turned a blind eye, the reason being that little can be done to prevent infection of the infant. If ARV treatments are introduced without sufficient preparation, women who seek termination of pregnancy may be denied this facility on the grounds that treatment is now available. These laws should now be amended to include an HIV positive status as an indication for termination of pregnancy.

**Obstetric Interventions**

Several interventions to reduce HIV transmission have been studied but only elective Caesarean section has so far been shown to be effective22. Because of the small number of pregnant women who know their HIV status, this intervention is well within the capabilities of maternity services in developing countries. It will only become unsustainable if a large proportion of women volunteer for antenatal testing for HIV. The fact that this intervention has not been fully implemented indicates that commitment has been lacking even for the proven interventions. It is possible that lack of protection for the staff and the non-availability of anti-retroviral prophylaxis for surgeons are contributing factors. Recently, concern has been raised regarding the safety of Caesarean section in HIV infected women23. The introduction of ARV regimens will lead to a decrease in the use of Caesarean section for MTCT prevention.

**Breastfeeding policies**

The HIV epidemic in sub-Saharan Africa has caused a re-appraisal of breastfeeding policies. Up to now, national ministries of health had only one policy for feeding infants after birth, namely, breast-only-feeding for at least six months, followed by the slow introduction of replacement feeding thereafter. In Zimbabwe, breastfeeding is recommended for 2 years. However, HIV transmission through breastfeeding is now known to be significant24. The families in the affected countries cannot afford replacement feeding and it is associated in their settings with diarrhoeal disease and other nutritional problems. For these reasons, governments in the region have been unable to
enunciate clear infant feeding policies. To add to the confusion, the published ARV regimens have been studied with breastfed and non-breastfed infants12-17.

Whereas in the private sector, the women can be individualised and offered all the different options available, in the public sector the effect of ARV regimens will be to narrow the infant feeding options to either one or two. Programmes can either implement ARV regimens with full breastfeeding only, or give the women a choice between full breastfeeding and full replacement feeding. Early cessation of breastfeeding, treatment of breast milk and wet nursing by a tested HIV negative woman27 are not viable alternatives. Mixed infant feeding is also not an option since there are reports that it is less safe than full breastfeeding28,29. The suggestion that there only be two infant feeding options recognises the lack of sophistication in public reproductive health programmes to implement, concurrently, several different regimes of breastfeeding. The infrastructure to train staff and monitor compliance with the several different protocols is non-existent. In many ways, starting with the infant feeding policies which can be implemented will simplify the choice between the ARV regimens available.

**Feasibility of ARV Regimens**

The feasibility of ARV regimens will depend on many factors but the most important will be the simplicity of the regimen, the acceptance by the women and the cost. Single doses are preferred to multiple ones and oral medications preferred to parenteral injections.

Among the regimens published so far, the HIVNET 012 protocol17 will be the easiest to implement, followed by the short Zidovudine courses used in Thailand12 and Côte d'Ivoire13. The differences between the latter two are that in Côte d'Ivoire the infants were breastfed, and some infants were given a shorter course of ARV treatment.

The regimens will have to be given through the existing maternity care structures and should not be separate programmes, otherwise education, monitoring of the compliance and maintenance of the supplies will not be sustainable. None of the above three regimens is too complicated to be taught to the nurses or midwives who deliver women in the primary health centres in sub-Saharan Africa.

Any important feasibility issue will be which women should be treated. If the prevalence of HIV infection in pregnant women is over 30%, should all of them be treated? A drug as cheap as nevirapine could conceivably be given in such a setting to all women except those who are HIV negative. Anti tetanus toxoid is given to all women to prevent a lesser risk of infant death. Of course the concerns about drug resistance, for instance in the case of nevirapine, would need to be addressed. ARV regimens are now available which together with other interventions reduce the risk of MTCT significantly. Some of them could be introduced into the reproductive health programmes of developing countries. The relevance and effectiveness of ARV regimens will depend on several key programmatic issues and how well they are addressed by national health ministries. A summary of such issues is shown in Table 1.
Table 1: Key programmatic issues which determine the effectiveness of ARV Treatment.

1. Adequate prevention of infection in women of reproductive age.
2. Adequate implementation of antenatal HIV counselling and testing.
3. Full provision of termination of pregnancy for HIV.
4. Adequate use of proven obstetric interventions.
5. A clear infant feeding policy should be announced.

References


11. To be inserted


21. To be inserted


