TLALELETSO

Prevention of Mother to Child Transmission

In this issue of Tlaleletso we review relevant research demonstrating the best ways to prevent mother to child transmission of HIV. We also review current practice in Botswana and discuss important policy changes that may be on the horizon.

INTRODUCTION

In 2009, there were approximately 370,000 new HIV infections in children in Africa and more than 90% of these infections were attributable to Mother to Child Transmission (MTCT). MTCT can occur during pregnancy, labor and delivery, or breastfeeding. Without treatment up to 30% of babies born to HIV-infected women will become infected. Up to 20% more become infected through breastfeeding.

In developed countries, maternal HIV transmission has been dramatically reduced due to effective testing and counseling, together with widespread access to ART, safe delivery practices and the availability of breast milk substitutes.

However, many of these interventions have not been widely available in Sub Saharan Africa until recently and consequently AIDS remains a major cause of infant death. Botswana has been at the vanguard of attempts to develop effective strategies to prevent mother to child transmission, even in the setting of high HIV prevalence.

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Notes from the Editor…..

Tlaleletso is a monthly publication produced by the Botswana UPenn Partnership, in response to your expressed need for accessible, digestible clinical information.

In this edition we review PMTCT and the best strategies for Botswana and Africa.

DID YOU KNOW?

Each year around 1.5 million women living with HIV become pregnant, and without antiretroviral drugs (ARVs), there is approximately 25 percent chance that their child will also become infected.

Basic principles of mother-to-child transmission of HIV

Without any intervention to prevent transmission, the rate of MTCT of HIV is estimated at 30%. MTCT of HIV can occur before, during and after birth. The relative contribution of each of these modes of perinatal transmission is not well defined. However, approximately 15% of transmissions occur during the antenatal/delivery period and 10% during breastfeeding.

Given these rates of transmission, numerous different strategies have been adopted to reduce MTCT. In high-income countries, strategies such as initiating ARVs in pregnant women, regardless of CD4 counts and performing Cesarean sections on all pregnant women, to reduce blood exposure to the infant at birth, are frequently performed. Such strategies have not been cost-effective or practical solutions in African settings, given the prevalence of HIV and the limited resources and money. However, in 2010 the world health organization recommended a set of strategies that offer realistic options for low resource settings. These are outlined below.

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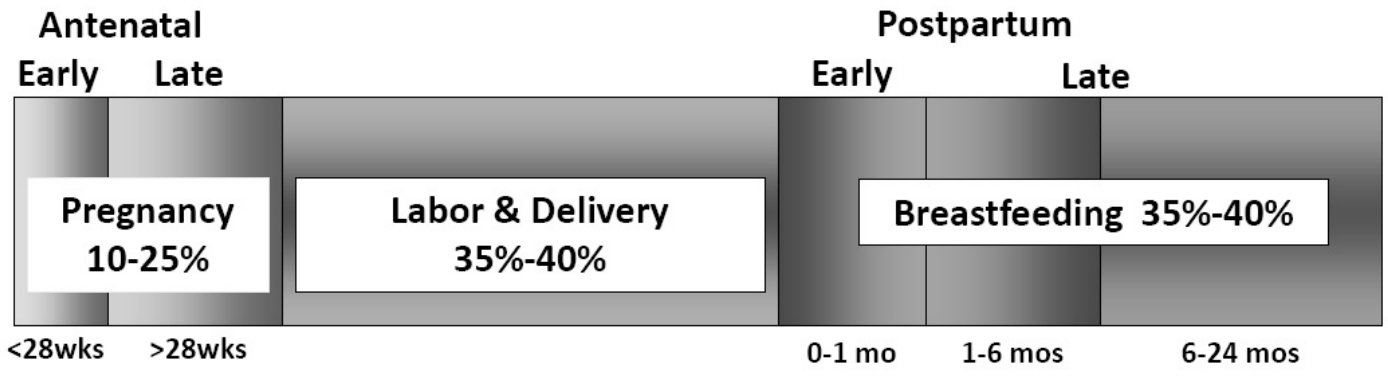
PMTCT – where transmission occurs…



As noted above, MTCT of HIV can occur before, during and after birth. Most transmission occurs either during labor and delivery or during the breastfeeding.

Basic principles of mother-to-child transmission of HIV?

Prior to 2006, WHO recommended that only women with a low CD4 count should receive a combination of antiretrovirals to prevent mother-to-child transmission. However, in 2010 new guidelines were published by WHO stating that all HIV-positive mothers, identified during pregnancy, should receive a course of antiretroviral drugs to prevent mother-to-child transmission.

Two treatment options were recommended - **Option A and Option B**. In those countries that adopted Option A, all pregnant women, ineligible for ARVs based on CD4 count, were to receive antepartum AZT from as early as 14 weeks, as well as intrapartum nevirapine and a first dose of AZT/3TC. Following delivery, these women would then receive AZT/3TC for a further 7 days.

Option B recommended giving triple ARV treatment from as early as 14 weeks gestation for all pregnant women regardless of their CD4 count. This treatment was to be continued until 1 week after cessation of breastfeeding or until childbirth if the women chose not to breastfeed.

The 2010 guidelines also recommended that all infants born to HIV-positive mothers should also receive a course of antiretroviral drugs and should be exclusively breastfed for 6 months and complementary fed for up to a year, regardless whether the mother received Option A or B. These recommendations were based largely upon on several studies, including two – the Mma Bana study and the Kesho Bora study both of which are described below:

Botswana was one of the first countries to adopt Option B – and has made triple ARV prophylaxis widely available to women who are not yet eligible for ARVs based on CD4 criteria. The current recommendations are that women should continue triple antiretroviral prophylaxis until 6 months post partum or until a month after stopping breast-feeding.

Did you know?

- About 1,000 babies were infected with HIV every day during pregnancy, birth or breastfeeding.
- Globally, there are approximately 1.4 million pregnant women living with HIV in low- and middle-income countries.
- Only 26% of pregnant women living in these countries received HIV tests.
- In Eastern and Southern Africa, the region hit hardest by the epidemic, only half of pregnant women were tested for HIV.
- An estimated 53% of pregnant women living with HIV in the developing world received antiretroviral drugs to prevent them from transmitting the virus to their babies.
- In Eastern and Southern Africa, 68% of pregnant women living with HIV received antiretroviral treatment.

Mma Bana Study

Past studies had shown that infant mortality rates were unacceptably high in Botswana and elsewhere in Africa if infants were fed with formula, rather than breast milk.

The *Mma Bana* (meaning "mother baby" in Setswana) Study was conducted at four clinical sites in Botswana as a collaboration between HAI and the Botswana government, in order to determine if HIV transmission could be prevented by providing ARVs to women who breastfed post partum.

The 730 HIV-positive women were given one of three different highly active antiretroviral therapy (HAART) regimens. The women began the drugs at about the third trimester of pregnancy and stayed on them through six months of breastfeeding. Their infants were tested for HIV infection/transmission at several intervals, including at birth and after six months of breastfeeding.

All HAART regimens used in the study were found to be highly effective at suppressing HIV viral load with a 95% viral suppression in the mother at delivery and 93% throughout breastfeeding. Two of the three drug combinations (Combivir/nevirapine and Combivir/Alluvia) gave particularly impressive results—one infant infection in each group during pregnancy and no infections during birth or through breastfeeding. The third combination drug, Trizivir, resulted in three infections during pregnancy and two during breastfeeding. The overall rate of infant infections in the study was 1%.

Before this study, many HIV-infected mothers in Botswana were faced with a choice between breastfeeding and a high risk of infecting their child with HIV, or using formula and risking high infant mortality from other diseases associated with not breastfeeding. The Mma Bana study clearly demonstrated that giving mothers HAART from early in the third trimester of pregnancy through six months of breastfeeding is a safe and effective strategy for preventing mother-to-child transmission of HIV while allowing for the benefits of breastfeeding

Kesho Bora Study

Giving a combination of three antiretrovirals to pregnant mothers with HIV from the last trimester through delivery and six months of breastfeeding reduces the risk of transmitting HIV to the baby and improves survival. The *Kesho Bora study* (a better future in Swahili) conducted in 5 sites in Africa, enrolled women with a CD4 count between 200 AND 500. The trial compared triple ARV regimen against zidovudine and single dose nevirapine stopped at delivery, which was the standard treatment recommended by the WHO from 2004

The triple ARV regimen cut infections in infants by 43% compared to the control regimen and reduced the risk of transmission during breastfeeding by more than half. There was no apparent risk to the health of the mothers or their babies associated with triple ARV regimen compared with the control regimen.

Findings from Kesho Bora strongly influenced the new WHO guidelines on PMTCT. These guidelines now recommend ARVs during breastfeeding for all women with HIV and continued ARV treatment for women with CD4 counts below 350 cells/mm.

(continued)

From PMTCT to EMTCT

In 2012, the World Health Organization released an update to the 2010 HIV and AIDS guidelines on PMTCT. The update outlined a change in recommendations for preventing mother-to-child transmission of HIV - **Option B+.** This approach is similar to Option B, but suggests giving the mother triple ARVs as soon as they are diagnosed, continuing for life, regardless of CD4 count.

Option B+ was first introduced in Malawi as a mechanism for Malawi to sidestep the necessity for CD4 testing of all pregnant women, involves placing all HIV-positive pregnant women on ART for life, regardless of CD4 count.

There are various benefits to this proposed strategy, the most obvious being that women on life-long therapy will be healthier with less risk of contracting opportunistic infections, leading to lower overall mortality. But equally important, Option B+ could also result in less HIV maternal-to-child-transmission, especially in subsequent pregnancies, leading to the potential end of pediatric HIV (as opposed to stop–start methods proposed with option A and B). Many clinicians believe that Option B+ represents the most realistic option for completely eliminating mother to child transmission (EMTCT).

The option B+ approach of lifelong ART for all HIV-infected pregnant women, regardless of CD4 count has important advantages over both existing options (A and B). These include:

1. Further simplification of the PMTCT program – no need to perform CD4 testing to determine ART eligibility or whether ART should be stopped or continued after the risk of mother to child transmission has ceased.
2. Extended protection from mother to child transmission in future pregnancies from conception
3. A strong and continuing prevention benefit against sexual transmission in sero-discordant couples and partners.
4. A likely benefit to the woman's health of earlier treatment and avoiding the risks of stopping and starting triple ARVs especially in settings with high fertility.
5. Improved communication with communities – since the message is simple to convey: once ART is started, it is taken for life.

Option B+ has not been endorsed in Botswana yet. While it offers programmatic, clinical and operational advantages and thus could serve to accelerate progress towards eliminating new pediatric infections, it will be a more expensive approach to PMTCT. Nevertheless, it will likely provide the best protection for the mother's health and it offers a more promising new approach to prevention sexual transmission and new HIV infections in the general population.

Other Important Issues…

Breastfeeding or Formula Feeding

As previously mentioned HIV transmission can occur at any point during breastfeeding. Although options such as exclusive formula feeding have demonstrated reduced risk of MTCT, a study performed in Botswana and published in 2006 clearly demonstrated that cumulative infant mortality 7 months after delivery was substantially higher in children who were formula fed compared to those who were formula fed in one recent study (Thior, 2006). This excess mortality was attributable to unsafe water used in the preparation of the infant formula.

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At present the Botswana government recommends formula feeding for all HIV-infected mothers who can ensure that formula feeding is Affordable, Feasible, Acceptable, Safe and Sustainable. However, since this is infrequently the case, especially in rural settings where a reliable supply of clean water cannot be guaranteed, many clinicians strongly advocate that breastfeeding is best, especially in women who are on triple ARV prophylaxis.

What about Efavirenz in pregnancy?

Clinicians frequently express concern about using EFV in pregnancy given the risks of teratogenicity. There is conflicting evidence of very low quality on the risks of EFV causing neural tube defects. In fact, data suggests that rates of overall birth defects in association with EFV are very similar to those in patients exposed to NVP and LPV/r and are consistent with rates reported in congenital defects in general populations. Current prospective data are insufficient to provide an assessment of neural tube defect risk with first trimester exposure, except to rule out a risk that is tenfold or higher than that in the general population. Since neural tube closure occurs by 28 days of gestation and very pregnancies are recognized by this time the potential risk with the use of EFV is primarily in women who become pregnant while already receiving the drug.

Summary

Prevention of Mother to Child Transmission strategies have been incredibly effective at reducing levels of HIV transmission in Africa. In Botswana the ministry of health recommends, triple ARV prophylaxis for all HIV-infected women who are not eligible for ARVs based on their CD4 counts, to be continued until after delivery or until a month the end of the period of breastfeeding. However, there is increasing groundswell of support for the Option B + strategy: lifelong ARVs for pregnant women regardless of CD4 count. This second option is undoubtedly a more expensive public health strategy. It is also undoubtedly more effective prevention intervention, especially for women that will go onto have more children!

Upcoming Lectures

August
Anemia & Anemia

September
Nutrition & HIV

October
Hepatitis & HIV

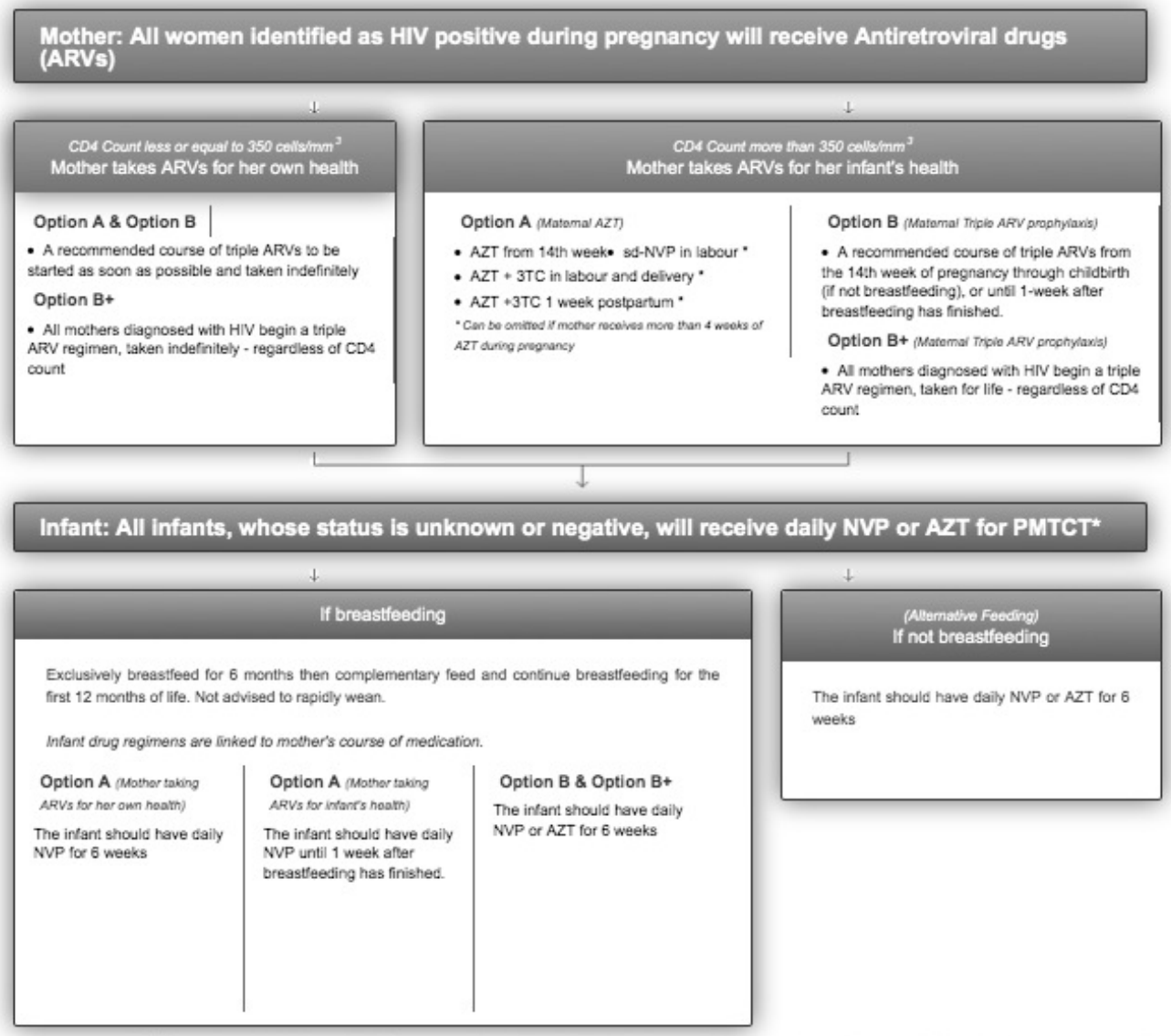
November
Neuropathy & HIV

Got a clinical question about a complicated medical patient or a patient with HIV?

Mike Reid
267 724 78 777
OR
Miriam Haverkamp
267 76516520

BOTSWANA-UPENN PARTNERSHIP

WHO approach to PMTCT



Please see WHO for guidance including details of recommended antiretroviral combinations and dosage levels etc. This page is intended to be a summary only. Please see your health worker for detailed advice.

Image courtesy of www.avert.org