

EMBARGOED until 14 January 2011, 01:01 Geneva time

Kesho Bora Study

Preventing mother-to-child transmission of HIV during breastfeeding

New evidence published in *Lancet Infectious Diseases* shows safety and efficacy of combination antiretroviral drugs during pregnancy, delivery and breastfeeding and supports the 2010 revised WHO guidelines.

Key points

1. Giving a combination of three antiretroviral (ARV) drugs to pregnant mothers with HIV infection from the last trimester, through delivery and six months of breastfeeding reduces the risk of transmitting HIV to the baby and improves survival.
2. These results are from the Kesho Bora study (a better future in Swahili) conducted in five sites in Africa which enrolled women with a CD4 count between 200 and 500 cells/mm³. The randomized trial compared the triple-ARV regimen against a control regimen of zidovudine and single-dose nevirapine stopped at delivery, which was the standard regimen recommended by WHO from 2004 (the “control” regimen).
3. The triple-ARV regimen cuts HIV infections in infants by 43% compared with the control regimen, and reduces the risk of transmission during breastfeeding by more than half.
4. This approach offers new hope for mothers with HIV infection who cannot safely feed their babies with infant formula. It will improve the chances of infants remaining healthy and free of HIV infection as breast milk provides optimal nutrition and protects against other fatal childhood diseases such as pneumonia and diarrhoea.
5. There is no apparent risk to the health of mothers or their babies associated with the triple-ARV regimen compared with the control regimen.
6. Infants of mothers whose virus is fully suppressed (undetectable) by triple-ARVs at the time of delivery have a very low risk of HIV infection (only 2.7% by the age of one year). It is therefore important to start ARVs early in pregnancy, ideally before pregnancy, for all women who require antiretroviral treatment (ART) (CD4 count at or below 350 cells/mm³). Giving HIV-positive pregnant women and those planning pregnancy priority access to HIV testing, CD4 count and ARVs will help eliminate mother-to-child transmission of HIV.
7. Findings from the Kesho Bora study strongly influenced the new WHO guidelines on antiretrovirals, prevention of mother-to-child transmission of HIV, and infant feeding that were issued in July 2010. These guidelines now recommend ARVs for mothers or babies during breastfeeding for all women with HIV and continued antiretroviral treatment for women with a CD4 count at or below 350 cells/mm³.

Kesho Bora Study

Preventing mother-to-child transmission of HIV during breastfeeding

In many developing countries, mothers with HIV have faced a stark choice: to breastfeed their babies, and risk passing on the virus through their breast milk; or to formula feed, and risk their infants dying from diarrhoea, pneumonia and malnutrition because they are deprived of the nourishment, natural immunity and protection of breast milk.

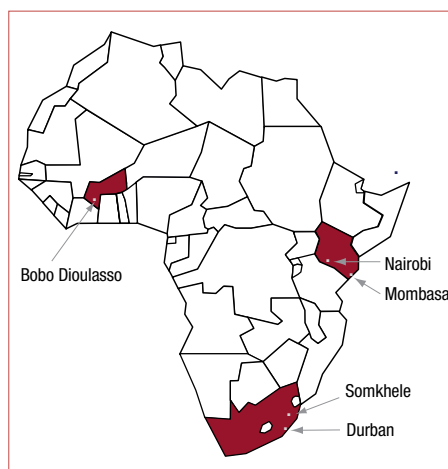
A study led by the World Health Organization's (WHO) Department of Reproductive Health and Research in partnership with the French National Agency for Research on AIDS and Viral Hepatitis (ANRS), US Centers for Disease Control and Prevention (CDC) and Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) of the National Institutes of Health, offers new insights and new hope for preventing HIV infection and death among infants in settings where many mothers with HIV infection breastfeed. The purpose of the study was to assess whether the risk of HIV transmission during breastfeeding could be safely reduced by providing a combination of three ARVs.

The findings of the Kesho Bora study show that the risk of HIV infection in breastfed infants is greatly reduced when mothers with a CD4 count between 200 and 500 cells/mm³ are given an extended triple-ARV regimen. The study treatment consisted of the anti-HIV drugs zidovudine, lamivudine and lopinavir/ritonavir, from the last trimester of pregnancy and continued during breastfeeding up to the age of six months.

The evidence for providing ARVs to pregnant women with HIV during late pregnancy and delivery to reduce transmission to their infants is well established. But this was the first randomized trial to directly compare the safety and efficacy of a combination of three ARVs given during pregnancy and continued during breastfeeding against the standard regimen recommend by WHO since 2004 of zidovudine started in late pregnancy and stopped after delivery, combined with single-dose nevirapine during labour. The balance of risks and benefits of continuing

ARVs during breastfeeding for mothers with an intermediate stage of HIV disease (CD4 count between 200 and 500 cells/mm³) was not known prior to this study.

Between June 2005 and August 2008, at five sites across Africa¹ researchers enrolled pregnant women with HIV infection. Women with a CD4 count below 200 cells/mm³ were given antiretroviral treatment; those with a CD4 count above 500 cells/mm³ (who have a low risk of transmission) were given the control prophylaxis stopping at delivery. 824 women with a CD4 count between 200 and 500 cells/mm³ were randomly assigned to one of two groups. In the intervention group, 412 women were provided with a combination of three ARVs for the last two months of pregnancy, through delivery and during breastfeeding (for a maximum of six months after delivery). The women were advised to stop all breastfeeding before they stopped taking ARVs. In the control group, the women were given a regimen of zidovudine and single-dose nevirapine, which stops one week after delivery and does not include further administration of ARVs to mother or infant during breastfeeding. Blood samples were taken from all infants for HIV testing at birth, and then periodically throughout the study, until they were 12 months old.



¹. Centre Muraz, Bobo-Dioulasso, Burkina Faso; University of Kwazulu Natal, Durban, South Africa; International Centre for Reproductive Health, Mombasa, Kenya; University of Nairobi, Kenya; and the Africa Centre for Population Studies, Somkhele, South Africa.

At 12 months of age, 9.5% of infants in the control group had acquired HIV, and a further 6.5% had died. By comparison, 5.4% in the triple-ARV group had acquired HIV and a further 4.8% had died. This corresponds to a 43% decrease in overall HIV infections, 54% reduction in transmissions during breastfeeding and a 36% decrease in HIV infections or deaths. The best results, with the largest number of infections averted, were in the group of women enrolled with a CD4 count between 200 and 350 cells/mm³. The number of adverse events was rare, with similar frequency in the two groups.

The Kesho Bora study shows that providing a combination of three ARVs to pregnant and breastfeeding mothers is a safe and effective way to reduce HIV transmission to infants, particularly those born to women with a CD4 count between 200 and 350 cells/mm³.

The new results published in *Lancet Infectious Diseases* on 14 January 2011 show that infants of mothers whose virus was fully suppressed (undetectable) by the ARVs at the time of delivery had a very low risk of transmission (only 2.7% infected by the age of one year). It is therefore important to start combination ARVs early in pregnancy, or even before pregnancy. Giving HIV-positive pregnant women and those planning pregnancy priority access to ARVs will help to eliminate mother-to-child transmission of HIV. About 80% of transmissions occur in women with CD4 counts below 350 cells/mm³. Therefore, universal coverage of antiretroviral treatment for all women with a CD4 count at or below 350 cells/mm³ has the potential to prevent over three-quarters of HIV infections in infants. For maximum efficacy, ART should ideally be initiated before pregnancy and therefore women planning to become pregnant should be strongly encouraged to have an HIV test and CD4 count.

WHO recommendations on the use of ARVs in pregnant women, including during the breastfeeding period, were reviewed in 2009 and new guidelines published in July

2010. The revision took account of all new data on HIV transmission during pregnancy and the breastfeeding period, including preliminary results from the Kesho Bora study. WHO now recommends providing ART to all pregnant women with CD4 count at or below 350 cells/mm³ and to provide ARV prophylaxis (either to the mother or to the child) for the entire duration of breastfeeding.

In the developed world, mothers with HIV avoid breastfeeding altogether and can instead feed their infants with formula. But in many low- and middle-income countries, formula feeding of infants is neither feasible nor safe. Sanitation is lacking, and clean water to mix formula is often not available. Many families cannot afford infant formula. It may be difficult to obtain enough fuel to boil the water to prepare formula safely. Formula-fed infants miss out on protective antibodies — passed on through breast milk — that ward off other deadly diseases. Formula feeding may also carry a social stigma in certain settings — the practice may be seen as a sign that a woman has HIV infection.

According to the revised WHO recommendations, national authorities should consider the likely circumstances of HIV-infected mothers attending health facilities and then decide whether breastfeeding with the protection of ARVs or avoidance of all breastfeeding and providing formula will give these infants the greatest chance of surviving and remaining free of HIV infection. Where breastfeeding protected with ARVs is promoted and supported, then breastfeeding should be exclusive (only breast milk, with no addition of water or food, as recommended for all breastfed infants) for their first six months of life and can be safely continued up to the age of 12 months with complementary feeding.

Study sponsors

The Kesho Bora study was a partnership between international and national research agencies and institutions. It was coordinated by WHO's Department of Re-

productive Health and Research. The majority of funds was provided by ANRS which supported and helped coordinate the sites in Bobo Dioulasso and Mombasa. NICHD and CDC jointly supported and coordinated the site in Nairobi. Additional funds for the research were provided by the European and Developing Countries Clinical Trials Partnership, the Thrasher Research Fund, the United Kingdom Department for International Development, UNICEF and the Belgian Government.

Related documents and additional information

The Kesho Bora Study Group. Triple antiretroviral compared with zidovudine and single-dose nevirapine prophylaxis during pregnancy and breastfeeding for prevention of mother-to-child transmission of HIV-1 (Kesho Bora study): a randomized controlled trial. *Lancet Infectious Diseases*, 2011; 11 (www.thelancet.com/infection), published online January 14, 2011 DOI:10.1016/S1473-3099(10)70288-7)

The Kesho Bora Study Group. Triple-antiretroviral prophylaxis during pregnancy and breastfeeding compared to short-ARV prophylaxis to prevent mother-to-child transmission of HIV-1: the Kesho Bora randomized controlled clinical trial in five sites in Burkina Faso, Kenya and South Africa. 5th IAS Conference on HIV Pathogenesis, Treatment & Prevention. Cape Town, South Africa, 19–22 July 2009. Abstract LBPEC01. <http://www.ias2009.org/pag/pdf/3631.pdf>

Antiretroviral Drugs for treating pregnant women and preventing HIV infections in infants: towards universal access. Recommendations for a Public Health Approach (2010 version). Geneva, World Health Organization, 2010. http://whqlibdoc.who.int/publications/2010/9789241599818_eng.pdf

WHO, UNAIDS, UNFPA, UNICEF. *Guidelines on HIV and infant feeding 2010: principles and recommendations for infant feeding in the context of HIV and a summary of evi-*

dence. Geneva, World Health Organization, 2010. http://whqlibdoc.who.int/publications/2010/9789241599535_eng.pdf

PMTCT strategic vision 2010–2015. Preventing mother-to-child transmission of HIV to reach the UNGASS and Millennium Development Goals. Geneva, World Health Organization, 2010. http://www.who.int/entity/hiv/pub/mtct/strategic_vision.pdf

WHO's Department of Reproductive Health and Research — information on the Kesho Bora study: <http://www.who.int/reproductivehealth/topics/rtis/mtct/en/index.html>

Contact

Dr Timothy Farley

Department of Reproductive Health and Research
World Health Organization, Geneva, Switzerland

Tel: +41 22 791 33 10,

Mobile: +41 79 254 68 32,

E-mail: farleyt@who.int



© World Health Organization, 2011

All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use.