World Health Organization

5th IAS Conference on HIV Pathogenesis, Treatment & Prevention anRS French National Agency for Research on AIDS and Viral Hepatitis

Cape Town, South Africa, 19-22 July 2009
BACKGROUNDER - KESHO BORA STUDY

Preventing Mother-to-Child Transmission of HIV During Breastfeeding

New evidence that giving mothers a combination of ARVs during pregnancy, delivery and breastfeeding cuts HIV infections in infants by 42% compared with current WHO recommendations

Key points
1. Giving a combination of three antiretroviral (ARV) drugs to pregnant mothers with HIV infection and CD4 count between 200 and 500 cells/mm3 from the last trimester, through birth and six months of breastfeeding reduces the risk of transmitting HIV to the baby and improves survival compared with babies of mothers with HIV who are given the current WHO-recommended short-course ARV regimen.
2. There is no increase in risk to the health of mothers or their babies associated with the triple-ARV regimen.
3. The biggest benefits in terms of HIV-free survival are among babies born to mothers with a CD4 count of between 200 and 350 cells/mm3.
4. These findings will be considered by WHO experts, together with other recent data on the use of ARVs to reduce HIV transmission during pregnancy and breastfeeding, when guidelines are updated later this year.
5. This approach offers new hope for mothers with HIV infection who cannot safely feed their babies with infant formula or other replacement foods.

In many developing countries, mothers with HIV face a stark choice: to breastfeed their babies, and risk passing on the virus through their breast milk; or to formula feed, and deprive their infants of the natural immunity transmitted through breast milk which helps protect against potentially deadly diarrhoeal disease and malnutrition.

A study led by the World Health Organization (WHO) 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, despite the risks. The purpose of the study was to assess whether the risk of HIV transmission during breastfeeding could be safely reduced.

The findings of the study named "Kesho Bora" ("a better future" in Swahili) 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 ARV regimen. The study treatment consisted of the anti-HIV drugs zidovudine, lamivudine and lopinavir/ritonavir, from the last trimester of pregnancy and continued for a maximum of six months of breastfeeding.

The evidence for providing ARVs to pregnant women with HIV during late pregnancy and delivery to reduce transmission of HIV to their infants is well established. But this is the first randomized trial to directly compare the safety and efficacy of an ARV combination given during pregnancy and continued while breastfeeding with the standard WHO-recommendation of a short-course of ARVs in late pregnancy and around the time of delivery.
The health of mothers was an important consideration in the design of the study. Based on the stage of the mother's HIV disease, different ARV regimens were prescribed. Women at an advanced stage of disease (CD4 count below 200 cells/mm3) need ARVs for their own health, and this treatment also sharply reduces the risk of passing on the infection to their babies. The risk of infection for children born to mothers with early stage HIV disease (CD4 count above 500 cells/mm3) is low and can be well-controlled with current WHO-recommended short-course prophylaxis. The balance of risks and benefits of continuing using 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 Africa[1], researchers enrolled 1,140 pregnant women with HIV. Women with a CD4 count below 200 cells/mm3, or experiencing symptoms of AIDS, were offered long-term ARV therapy (in line with current WHO recommendations). Women enrolled with a CD4 count above 500 cells/mm3 were offered the current WHO-recommended ARV prophylaxis regimen until one week after delivery. Women with a CD4 count between 200 and 500 cells/mm3 were randomly assigned to one of two groups. In the first, or "intervention" group, 413 women were provided with a combination of three ARVs for the last two months of pregnancy, through delivery and while breastfeeding (for a maximum of six months after delivery). The women were advised to stop all breastfeeding before they stopped taking ARVs. In the second, or "standard" group, the women were given the standard WHO-recommended short-course of ARVs, 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.

At 12 months of age, 9.5% of infants in the "standard" group had acquired HIV, and 16.3% were either HIV-infected or had died. By comparison, 5.5% in the "intervention" group had acquired HIV and 10.4% were either HIV-infected or had died. This corresponds to a 42% decrease in

HIV infection 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 — that is, those who, according to current recommendations, are not yet considered to need ARVs for their own health. The number of adverse events was rare, with similar frequency in the two groups.

The study authors concluded that providing the combination of three ARVs to breastfeeding mothers is a safe and effective way to reduce HIV infection among infants, especially those born to women with a CD4 count between 200 and 350 cells/mm3. The mothers and babies in the study are still being followed to assess the long-term safety of the intervention.

The 2006 WHO recommendations on the use of ARVs in pregnant women, including during the breastfeeding period, are currently being reviewed, and it is expected that new guidelines will be published by the end of 2009. The revision process takes account of all new data since the last revision, including those presented at the IAS 2009 conference.

In the developed world, mothers with HIV avoid breastfeeding and instead feed their infants with formula. But in many poor countries, there are barriers to formula feeding. Sanitation is lacking, and clean water to mix formula is often not available. Many families have difficulty affording infant formula. They also have difficulty providing enough wood or charcoal for cooking fires to boil water needed for formula.
Formula-fed infants also miss out on protective antibodies — passed on through breast milk — needed to ward off other deadly diseases. Formula feeding may also carry a social stigma for mothers in certain settings — the practice is often seen as a sign that a woman has HIV infection.

According to current WHO recommendations, exclusive breastfeeding is recommended for babies of HIV-infected women for their first six months of life, unless formula feeding is acceptable, feasible, affordable, sustainable and safe before that time. If an HIV-infected woman chooses to breastfeed, exclusive breastfeeding (only breast milk, with no addition of water or foods) for the first six months is recommended. WHO recommendations on infant feeding are also being reviewed in the context of new ARV guidelines for the prevention of mother-to-child transmission of HIV, and will also be published by the end of 2009.

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 Reproductive Health and Research, but the majority of the financial support 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 Foundation, the UK Department for International Development, UNICEF and the Belgian Government.

Related documents and additional information

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.

Antiretroviral Drugs for Treating Pregnant Women and Preventing Infections in Infants: Towards Universal Access. Recommendations for a Public Health Approach (2006 version)
English: http://whqlibdoc.who.int/publications/2006/9789241594660_eng.pdf
French: http://whqlibdoc.who.int/publications/2007/9789242594669_fre.pdf

Conclusions of the WHO expert consultation on new and emerging evidence on the use of antiretroviral drugs for the prevention of mother-to-child transmission of HIV, 17-19 November 2008, Geneva, Switzerland
http://www.who.int/child_adolescent_health/documents/media/pmtct_consultation_2008.pdf

Consensus Statement on HIV and Infant Feeding by the Inter-Agency Task Team on Prevention of HIV Infections in Pregnant Women, Mothers and their Infants, October 2006
English:
http://www.who.int/child_adolescent_health/documents/pdfs/who_hiv_infant_feeding_technical_consultation.pdf
French:
http://www.who.int/child_adolescent_health/documents/pdfs/who_hiv_infant_feeding_technical_consultation_fr.pdf

United Nations agencies' HIV and Infant Feeding Framework for Priority Action
English: http://whqlibdoc.who.int/publications/2003/9241590777_eng.pdf
French http://whqlibdoc.who.int/publications/2004/9242590770.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

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South Africa; International Centre for Reproductive Health in Mombasa, Kenya; University of Nairobi, Kenya; and the Africa Centre for Population Studies in Somkhele, South Africa.