WORLD HEALTH ORGANIZATION

WHO Expert Consultation on
New and emerging evidence on the use of antiretroviral drugs
for the prevention of mother-to-child transmission of HIV
Geneva, 17-19 November 2008

CONCLUSIONS OF THE CONSULTATION

The World Health Organization (WHO) convened an expert consultation to review new evidence on the use of antiretroviral drugs to prevent mother-to-child transmission of HIV (PMTCT) as well as on-going research likely to yield new data in the next 6 to 12 months. A particular focus was placed on reviewing data on interventions to reduce transmission of HIV through breastfeeding. The purpose of the consultation was to analyse these findings and identify gaps in the current evidence base, in order to clarify the necessary steps and timelines for the revision of WHO guidelines on PMTCT.

Background

About 370,000 children younger than 15 years of age worldwide become infected with HIV in 2007[1]. The overwhelming majority of these children are infected as a result of transmission of the virus from HIV-infected mothers during pregnancy, childbirth or breastfeeding. Most of these mothers and children live in sub-Saharan Africa where infant, child and maternal mortality rates are generally high.

The 2006 WHO guidelines on antiretroviral (ARV) drugs for treating pregnant women living with HIV and preventing HIV infections in infants[2] take account of the intimate relationship between maternal health and child survival. Early identification of pregnant women living with HIV who require antiretroviral therapy (ART) for their own health and successful initiation of such drugs will improve the health and survival of mothers and significantly reduce infant and child mortality. Data from cohorts in Europe and North America demonstrate what can be achieved in well-resourced health systems and communities. Providing HIV-infected pregnant women with ART or combination ARV prophylaxis according to respective eligibility criteria has substantially reduced the risk of infants becoming infected during pregnancy and delivery. When combined with elective Caesarean section and avoidance of all breastfeeding, these interventions have reduced the risk of HIV transmission to infants to approximately 1%. In resource-limited settings, similarly low rates of peripartum transmission (2-5%) have been reported in some research and pilot programmes.

Unfortunately the results of PMTCT services in many national programmes, have been less encouraging. Low rates of HIV testing among pregnant women, lack of availability and access to PMTCT services, and difficulties integrating PMTCT interventions within existing maternal and child health (MCH) services compounded by human resource constraints have contributed to the slow pace of expansion of PMTCT coverage. Countries' transition from providing only single dose nevirapine (sdNVP) to the mother during labour and the infant after birth to more efficacious combination prophylaxis regimens has also been slow. In addition, reducing the risk of postnatal transmission via breastfeeding has remained a significant challenge. As a result there has been a limited reduction in the number of paediatric HIV infections.

Meeting participants and content

Participants of the WHO expert consultation included researchers and programme experts. Together they reviewed the results of studies on whether ARVs delivered to HIV-infected breastfeeding mothers, or to their infants during the period of breastfeeding, reduce the risks of transmission and allow infants to gain the benefits of breastfeeding and thereby improve HIV-free survival. The designs and preliminary results of other ongoing or planned studies were also reviewed. See table below.

WHO process of developing or updating guidelines includes the systematic review of randomized and observational studies and programme data to assess the efficacy and effectiveness of interventions[3]. New recommendations are based on thorough review of evidence of efficacy and safety of interventions, modelling of the cost and impact of different scenarios to assess the advantages of any given intervention against its potential for harm, and detailed assessments of its acceptability, cost and feasibility for delivery within health care systems.

[1] UNAIDS. Global AIDS Epidemic Report 2008
[2] WHO. Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: towards universal access. Recommendations for a public health approach. 2006. http://www.who.int/hiv/pub/guidelines/pmtct/en/index.html

[3] WHO Handbook for Guideline Development. March 2008.

Studies reported in peer-reviewed journals, international conferences or that are ongoing / planned

Studies that have been reported or presented

AMATA	Observational cohort of HIV+ mothers given ARVs antenatally and while breastfeeding
DREAM	Observational cohort of HIV+ mothers given ARVs antenatally and while breastfeeding
MITRA +	Observational cohort of HIV+ women given ART antenatally and while breastfeeding
KiBS	Observational cohort of HIV1 mothers given ARVs antenatally and while breastfeeding
MASHI	RCT* of AZT to breastfeeding infants compared to replacement feeds in other HIV-exposed infants
MITRA	Observational cohort of 3TC to infants while breastfeeding
ZEBS	RCT* of counselling of mothers for early cessation vs. continued breastfeeding
SWEN	RCT* of NVP for 6 wks compared with placebo for infants while breastfeeding
PEPI	RCT* of NVP for 3 mo compared to placebo for infants while breastfeeding

Ongoing

BAN	RCT* of triple ARVs to mothers or NVP to infants during breastfeeding
Kesho Bora	RCT* of triple ARVs compared with short-course ZDV+sdNVP to mothers during pregnancy and breastfeeding
Mma Bana	RCT* of two different triple- combination ARVs to mothers during pregnancy and breastfeeding
HPTN 046	RCT* of NVP for 6m compared to 6wks to infants while breastfeeding

Planned

PROMISE PEP	RCT* of 3TC compared to placebo for infants while breastfeeding
PROMISE (NIH)	RCT* of ARVs to mothers or infants during pregnancy and breastfeeding
Universal maternal ART	ART to all pregnant women during pregnancy and while breastfeeding

*RCT – Randomised controlled trial

Outcomes of studies were reviewed in terms of: HIV transmission and HIV-free survival; resistance and subsequent responses to ART; feasibility of interventions; morbidity and mortality of infants who stop breastfeeding; birth outcomes; and harmonization of guidelines, in this case PMTCT guidelines, with WHO adult and paediatric treatment guidelines.

The results of these studies are very promising and suggest that new intervention strategies may substantially lower the risk of HIV transmission to infants during pregnancy, delivery and breastfeeding. However, the evidence is insufficient to fully assess which interventions are the most effective, feasible and safe for mothers and infants if implemented within health care systems. Additional data will become available in the next nine months. WHO will actively collaborate with investigators to assess their significance in order to revise recommendations at the earliest appropriate time.

The participants strongly recommended the following actions:

In guideline development

- WHO-recommended eligibility criteria for initiating ART for pregnant women own health be urgently reviewed with a view to earlier initiation;
- WHO recommendations for infant ARV prophylaxis be urgently reviewed
- Further simplifications of existing guidelines be considered in order to facilitate country implementation;

In service delivery

- PMTCT services prioritize identifying HIV-infected pregnant women who fulfil current eligibility criteria for lifelong ART in order rapidly to initiate comprehensive treatment and care;
- For HIV-infected pregnant women who do not fulfil these criteria, PMTCT services should work to provide WHO recommended PMTCT interventions that are more efficacious than sdNVP only;
- HIV-infected mothers receive high quality counselling with respect to infant feeding options;
- PMTCT services be fully integrated into MCH services and linked with HIV treatment sites;
- Further work be conducted to address implementation problems that threaten the quality and impact of PMTCT services, beyond the choice of ARV regimens for therapy or prophylaxis;

In research

- Research continue in order to identify the most effective, safe and feasible interventions to prevent transmission of HIV to infants during pregnancy, childbirth and while breastfeeding;
- Implementation research be conducted to learn how to deliver integrated PMTCT services more effectively and link with follow-up care and treatment of mothers and infants;
- Monitoring and evaluation data be collected and reported to inform the feasibility and population impact of PMTCT interventions.

A full revision of WHO recommendations for PMTCT is anticipated in mid-late 2009.

These conclusions do not necessarily represent the decisions or policies of the World Health Organization.

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