HIV Transmission Through Breastfeeding

A REVIEW OF AVAILABLE EVIDENCE

2007 Update

World Health Organization

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WHO Library Cataloguing-in-Publication Data

HIV transmission through breastfeeding : a review of available evidence : 2007 update.

1.HIV infections - transmission. 2.Acquired immunodeficiency syndrome - Transmission. 3.Breast feeding - adverse effects. 4.Disease transmission, Vertical - prevention and control 5.Review literature. I.World Health Organization.

ISBN 978 92 4 159659 6 (NLM classification: WC 503.3)

Printed in France.

Table of contents

Preface v

Acknowledgements vii

Acronyms viii

Glossary ix

Executive summary **1**

Introduction **3**

Mother-to-child transmission of HIV **5**

HIV infection in women 5

Rates of, and risk factors for, overall mother-to-child transmission 5

Prevention of mother-to-child transmission of HIV 6

HIV transmission through breastfeeding **9**

Pathogenesis and mechanisms of breastfeeding transmission 9

Risk of postnatal transmission through breastfeeding 10

Timing of postnatal transmission through breastfeeding 10

Early postnatal transmission through breastfeeding 10

Late postnatal transmission through breastfeeding 11

Factors associated with risk of transmission through breastfeeding 12

Maternal factors 12

Infant factors 16

Benefits of breastfeeding **19**

Health benefits of breastfeeding in the general population 19

Maternal health benefits 19

Child health benefits 19

Health benefits of breastfeeding in children born to HIV-infected mothers 21

HIV-exposed children, regardless of HIV status 21

HIV-infected children 21

Global breastfeeding practices 22

Strategies to reduce HIV transmission through breastfeeding **23**

Primary prevention of HIV in women of childbearing age 23

Framework to assess interventions to prevent postnatal transmission 24

Modifying infant feeding options for HIV-infected women: replacement feeding 24
Adverse outcomes of alternatives to breastfeeding practices 25
Social acceptability of feeding practices 25
HIV-infection 32
HIV-free survival 32
Discussion 32
Strategies for HIV-infected women who breastfed 33
Exclusive breastfeeding 33
Early cessation of breastfeeding 35
Heat treatment or pasteurization of expressed breast milk. 36
Microbicide treatment of expressed breast milk 36
Antiretroviral therapy during breastfeeding 37
Immunization of breastfed newborns 39
From research to public health recommendations on infant feeding: consequences for practice 39
Ongoing or planned research addressing the breastfeeding period 41
Conclusion 43
References 44

Preface

This Review was originally prepared as a back ground paper for the Technical Consultation on HIV and Infant Feeding that took place in Geneva in October 2006. It was updated during 2007 to include relevant new information.

As the Review was going to print at the beginning of 2008, several trials were underway to assess use of extended maternal or infant antiretrovirals to reduce transmission among HIV-exposed breastfed infants. Relevant findings were presented at the 15th Conference on Retroviruses and Opportunistic Infections (CROI) held from 3 to 5 February 2008 and are summarized here.[1]

Postnatal HIV transmission, infant outcomes and infant feeding practices

In a pooled analysis of individual data from a South African and a West African cohort study (abstract #46), the overall risk of postnatal HIV infection was 3.9% among children breastfed for <6 months and 8.7% among children breastfed for >6 months (adjusted hazard ratio: 1.8). Breastfeeding duration, as well as maternal immune status, appear to be major determinants of HIV transmission. The risk did not differ between exclusively and predominantly breastfed children. Exposure to breastfeeding mixed with solids during the first 2 months increased the postnatal risk of acquisition of HIV (adjusted hazard ratio: 2.9).

In the Vertical Transmission Study in South Africa (abstract #636), 18-month HIV-free survival of children of HIV-infected women shows that breastfeeding of HIV-uninfected infants beyond 6 months of age increases the risk of HIV acquisition without gains for survival. It remains important to identify means of making breastfeeding safer for HIV-infected women who have no choice other than to continue breastfeeding.

In a study on mastitis in Zambia (abstract #650), breast milk samples were collected from 38 women who had clinical symptoms of mastitis. The study found that during mastitis, elevations of breast milk viral load are restricted to the mastitic breast and eventually return to baseline levels, supporting current recommendations for women with mastitis to breastfeed from the unaffected breast.

Maternal outcomes and infant feeding practices

In the Ditrame-Plus cohort study in Abidjan (abstract #73), the risk of pregnancy before 12 months post-partum was comparable in replacement feeding and breastfeeding groups: 4%. Between 12 and 24 months post-partum, the risk of pregnancy was significantly lower among replacement feeders than breastfeeders. Replacement feeding was not responsible for a greater incidence of pregnancies in this West African urban context, probably due to the systematic offer and the frequent use of contraceptive services.

Antiretrovirals in breastfeeding women

The Kisumu Breastfeeding Study in Kenya (abstract #45LB) was an observational prospective cohort of children of lactating women taking antiretroviral treatment (ART) to prevent mother-to-child transmission (MTCT). Overall transmission rates were 3.9% at 6 weeks, 5% at 6 months, 5.9% at 12 months and 6.7% at 18

[1] CROI abstracts are available at http:/www.retroconference. org, accessed February 15, 2008.

months. There was no difference in HIV transmission by baseline maternal CD4 count. For those infants who became infected during the first 6 weeks of life, resistance was initially not detected (abstract #84LB), but emerged during the breastfeeding period.

In the MASHI trial in Botswana (abstract #637), the MTCT rate at one month was 1.2% among breastfeeders and 1.1% among formula feeders. The authors concluded that breastfeeding was not a risk for MTCT within the first month of life for children exposed to maternal ART and receiving infant antiretroviral prophylaxis.

The preliminary results of the non-randomized part of the Kesho-Bora study being conducted in five African sites (abstract #638) showed that the HIV transmission rate at 12 months was 7.6% in women with <200 CD4 with no significant difference according to infant feeding pattern; the rate was 5.8% among women with >500 CD4 count, respectively 7.5% and 0% in ever and never breastfed infants.

In the Dream cohort in Mozambique (abstract #369), 341 mother-infant pairs were followed from pregnancy until 12 months post partum; mothers breastfed while receiving ART until 6 months post delivery. ART continued beyond 6 months in women who initiated it for their own health. The HIV MTCT rates were: 1.2% (4) at birth, 1.9% (6) at 6 months, and 2.8% (8) at 12 months. Four late post-natal HIV-1 infections (>1 month of age) were observed in this cohort; 15% were lost to follow-up.

The Breastfeeding, Antiretroviral and Nutrition (BAN) Study in Malawi (abstract #648) reports on antiretroviral concentrations. Infants' plasma concentrations for all antiretrovirals were well below levels required for treatment, suggesting minimal risk for drug toxicity. Lamivudine (3TC) and nelfinavir exposure in infants would suggest minimal risk for resistance in HIV-infected children; however, low-level nevirapine (NVP) exposure via breast milk may predispose HIV-infected infants to resistance.

Antiretrovirals in breastfed children

The PEPI-Malawi Study (abstract #42LB) evaluated in a randomized controlled trial if 14 weeks of extended daily infant antiretroviral prophylaxis with NVP (group 2) or NVP+ZDV (group 3) with breastfeeding cessation from age 4-6 months would reduce postnatal transmission of HIV compared to controls receiving single dose (sd) NVP and one week ZDV (group 1). At age 9 months, the risk of HIV infection was 10.6% in group 1, 5.2% in group 2 and 6.4% in group 3. However, at 18 months, the HIV rate reach 13.9% in group 1, 10.1% in group 2 and 10.2% in group 3. Postnatal transmission occurred after NVP cessation among breastfed children. Post-exposure prophylaxis in breastfed children could reduce postnatal transmission but should be maintained over the entire breastfeeding duration.

In the SWEN randomized controlled Trial conducted in Ethiopia, India and Uganda (abstract #43), an extended infant post-exposure prophylaxis with daily NVP for 6 weeks in breastfed infants of HIV-infected mothers was assessed. The 6-week HIV transmission rate in the extended-NVP arm was 2.5% versus 5.3% in the sd NVP arm (p=0.009), but the 6-month HIV rate was 6.9% in the extended-NVP arm versus 9.0% in the sd NVP arm (p=0.16). The extended-NVP arm was safe, but postnatal transmission occurred after stopping NVP in breastfed children with a reduction of long term efficacy. Occurrence of resistance to NVP in infected children was very high (11/12).

Acknowledgements

This review was updated by Valériane Leroy (INSERM U593, Institut de Santé Publique, Epidémiologie et Développement, Université Victor Segalen, Bordeaux, France). It is based on an original review on HIV transmission through breastfeeding prepared by Marie-Louise Newell (Institute of Child Health, London) for WHO in 2003. The 2003 review was updated in 2005 by the WHO Department of Nutrition for Health and Development as a background paper for a consultation on Nutrition and HIV.

We are very grateful to Marie-Louise Newell for helping in structuring the early draft of this review and to Lynne Mofenson for providing useful information on synthesis of the technical consultation. We would like to especially thank Rajiv Bahl, Renaud Becquet, André Briend, Anirban Chatterjee, Anna Coutsoudis, François Dabis, Mary Glenn Fowler, Peggy Henderson, Lida Lhotska, Jose Martines, Ellen Piwoz, Felicity Savage, Constanza Vallenas and Isabelle de Vincenzi for reviewing the report and giving helpful comments. Finally, we would like to acknowledge the contributions of Coralie Thore, Christian Weller and Evelyne Mouillet from the ISPED library in Bordeaux for their help in researching papers.

Kai Lashley performed the final copy-edit of the text.