Interventions for preventing late postnatal mother-to-child transmission of HIV

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Complete avoidance of breastfeeding prevents mother-to-child transmission of HIV, but in settings where clean water is not available, this intervention carries a similar risk of infant mortality to that among breastfed infants. Mixed infant feeding is associated with the highest risk of postnatal mother-to-child transmission of HIV through breast milk. Extended (14 weeks) antiretroviral prophylaxis given to both the mother and her breastfeeding baby reduced the risk of mother-to-child transmission of HIV.

RHL Commentary by Mnyani CN

1. INTRODUCTION

Each year an estimated 150,000 infants are infected with HIV-1 through breastfeeding. The vast majority of these transmissions occur in under-resourced settings (1). Breastfeeding is a well recognized significant route of mother-to-child transmission of HIV. The World Health Organization recommends that 'where replacement feeding is acceptable, feasible, affordable, sustainable and safe, HIV-infected women should avoid breastfeeding' (2). However, in many low- and middle-income countries, these criteria for replacement feeding are not met, and breastfeeding remains the only option available to most HIV-infected women. Earlier guidance for HIV-infected women who elected to breastfeed recommended exclusive breastfeeding for the first 6 months of the infant’s life, followed by rapid weaning, thereby decreasing the duration of exposure to breast milk and hence lowering the risk of HIV transmission (3). However, research subsequently showed that, in under-resourced settings, rapid weaning was associated with increased infant morbidity and mortality. Hence, it is now recommended that if criteria for replacement feeding are not met at 6 months, breastfeeding should continue along with the introduction of complementary foods (2).

One of the research priorities in the area of prevention of mother-to-child transmission of HIV has been to find interventions to decrease late postnatal transmission via breastfeeding. The purpose of this review (4) was to assess the efficacy of different interventions to reduce late postnatal mother-to-child transmission of HIV as reflected by the HIV status of the child, overall survival and HIV-free survival.

2. METHODS OF THE REVIEW

The criteria for selection of studies for the review were rigorous and are clearly explained in the review by the authors. Diagrams are used in the review to explain the selection process and assessment of possible sources of bias in studies identified for inclusion. The types of participant, prevention and outcome measures were part of the inclusion criteria and, where additional information was required for the selection process,
attempts were made to contact the study authors to obtain clarity. A clear and detailed description of the included studies and their main outcomes are provided in the review.

3. RESULTS OF THE REVIEW

A total of seven studies (six randomized clinical trials and one intervention cohort study) met the inclusion criteria. Information on the number of participants was available for six of them. Complete data were available for a total of 8717 HIV-exposed infants, and all the participants were from low-and middle-income countries. Two of the six trials were conducted before antiretroviral prophylaxis for prevention of mother-to-child transmission of HIV became available in the countries where the studies were done. In four of the six randomized controlled trials, pregnant women and their infants received single-dose nevirapine only, and in one, short-course zidovudine starting at 34 weeks of pregnancy was given. Three of the randomized controlled trials compared breastfeeding of varying duration with formula feeding to assess the frequency of HIV transmission, overall survival and HIV-free survival. In one trial formula feeding was associated with a lower cumulative probability of HIV infection at 24 months, 20.5% [95% confidence interval (CI) 14.0%–27.0%] compared with 36.7% (95% CI 29.4%–44.0%) in breastfed infants. This study was conducted prior to the availability of antiretroviral drugs for prevention of mother-to-child transmission of HIV.

Mixed feeding was found to be associated with the highest risk of MTCT of HIV [hazard ratio (HR) 10.87; 95% CI 1.51–78.00]. Exclusive breastfeeding was associated with a lower risk of transmission than mixed feeding. However, early rapid weaning was associated with increased morbidity and mortality and no change in HIV-free survival; infants who were exclusively breastfed for only 4 months, followed by rapid weaning, had a postnatal HIV transmission risk of 6.2% compared with 8.8% in those who were breastfed for 6 months and more.

Three of the trials in the review assessed the efficacy of extended antiretroviral prophylaxis in breastfed infants. Different regimens of varying duration were used in the studies. Extended antiretroviral prophylaxis was found to decrease the risk of transmission via breast milk, with an HIV transmission rate of 5.2% in infants who received 14 weeks of nevirapine prophylaxis and 6.4% in those who received 14 weeks of dual prophylaxis of zidovudine and nevirapine. These transmission rates were significantly lower than the transmission rate of 10.6% in those who received the standard prophylaxis of single-dose nevirapine and 1 week of zidovudine. However, in another trial, in which antiretroviral prophylaxis of a shorter duration was used, HIV transmission rates were similar in those who received single-dose nevirapine and those who received extended prophylaxis of 6 weeks of nevirapine [relative risk (RR) 0.80; 95% CI 0.58–1.10].

One trial evaluated the effect on mother-to-child transmission rates of the use of vitamin supplementation in HIV-infected pregnant women. It was found that multivitamins, except vitamin A, had no effect on the overall risk of HIV transmission. Vitamin A was found to be associated with an increased risk of HIV transmission (RR 1.38; 95% CI 1.09–1.76).

4. DISCUSSION

4.1 Applicability of the results

Exclusive formula feeding is associated with the lowest risk of postnatal mother-to-child transmission of HIV. However, with this feeding practice there is an increased risk of infant morbidity and mortality, mainly from diarrheal and respiratory infections, resulting in decreased overall infant survival. Mixed infant feeding is associated with the highest risk of postnatal mother-to-child transmission of HIV via breast milk.

The interventions that have been shown to be efficacious in decreasing late postnatal transmission, namely exclusive formula feeding, exclusive breastfeeding and extended antiretroviral prophylaxis throughout the
breastfeeding period, require significant financial resources and staff time and skills. Although all the studies reviewed were conducted in under-resourced settings, the resources required for the interventions may not be readily available in these settings.

4.2 Implementation of the intervention

Owing largely to a lack of resources, implementation of some of the interventions to decrease HIV transmission via breast milk may not be feasible in many under-resourced settings. For example, a guaranteed supply of infant formula milk and other resources (clean water and fuel to boil the water) needed to make safe feeds for the baby remain largely unavailable to large segments of the population in many middle- and low-income countries. Exclusive breastfeeding requires intensive counselling and ongoing support, and it has been shown that even in ideal trial settings long-term adherence to a single infant feeding option, especially exclusive breastfeeding, is often low (5). The financial costs of antiretroviral drugs and of the infrastructure needed to support their provision may also be prohibitive in developing countries.

Preliminary results from a recently concluded multicentre trial (not included in this review) show that the risk of HIV infection in breastfed infants is greatly reduced when mothers with CD4 cell counts of between 200 and 500 cells/mm³ are given an extended antiretroviral regimen (6). The treatment in the study consisted of the anti-HIV drugs zidovudine, lamivudine and a lopinavir/ritonavir combination, administered from the last trimester of pregnancy and continued for a maximum of 6 months of breastfeeding. This is the first randomized trial to compare directly the safety and efficacy of an antiretroviral combination given during pregnancy and continued postnatally during breastfeeding with the standard WHO recommendation of a short-course of antiretrovirals administered in late pregnancy and around the time of delivery. Findings of this study are expected to lead to revision of the WHO recommendation regarding use of antiretroviral regimens for the prevention of postnatal mother-to-child transmission of HIV. Since concerns have been expressed about the possible adverse effects of extended prophylaxis and development of drug resistance in children who become infected with HIV, the findings of this study, which also looked into safety of the regimen, will be of great importance in the provision of effective strategies to reduce mother-to-child transmission of HIV whenever possible, despite the above constraints.

4.3 Implications for research

Data are needed on the long-term safety of the extended antiretroviral prophylaxis regimens used in mothers and babies in the recently conducted trials. This information will add to the knowledge on the use of combination antiretroviral therapy in breastfeeding women who do not yet require treatment for their own health. The information will enable interventions to be designed and adapted to suit the needs of HIV-infected mothers and their infants in under-resourced settings (5).

References

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. Poster presented at the 5th IAS Conference on HIV Pathogenesis, Treatment and Prevention, 19-22 July 2009, Cape Town, South Africa; http://www.who.int/entity/reproductivehealth/topics/rtis/Kesho_Bora_post...