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Evidence Assessment: Summary of a Systematic Review

Who is this summary for?
For Health Personel, managers of health facilities and stakeholders involved in the prevention of mother-to-child transmission of HIV.

Antiretroviral interventions for preventing breast milk transmission of HIV

Key findings

- Antiretroviral prophylaxis during breastfeeding, administered to the mother or HIV-exposed infant is efficacious in reducing mother-to-child transmission of HIV.
- Extended nevirapine alone or (14 weeks) with reduces the risk of HIV infection at 24 months in infants compared to single dose nevirapine plus one week of zidovudine
- Triple antiretroviral prophylaxis during pregnancy and breastfeeding reduces the risk of HIV transmission or death at 12 months when compared to a short regimen.
- Extended nevirapine for 6 weeks compared to single dose nevirapine reduces the risk of HIV infection or death at 6 months

Background

Worldwide, the primary cause of human immunodeficiency virus (HIV) infection in children is mother-to-child transmission (MTCT). MTCT of HIV can occur during pregnancy, around the time of delivery, or through breastfeeding. Great strides have been made in reducing MTCT during pregnancy and around the time of delivery. However, without intervention a significant proportion of children born to HIV-infected mothers acquire HIV through breastfeeding.

Question

What is the efficacy and safety of antiretroviral therapy (ART) prophylaxis in HIV-infected women or their breastfeeding infants in preventing MTCT of HIV?

Antiretroviral interventions for preventing breast milk transmission of HIV in Cameroon: The prevalence of HIV in Cameroon is 4.3% (5.6% for the women and 2.9% for the men). The national PMTCT program was launched in 2002. Many studies have been conducted in Cameroon and showed that the multidrug antiretroviral regimens (Zidovudine, Nevirapine in a single dose, Lamivudine) were feasible and resulted in low MTCT rates under routine conditions. The Option B+ (systematic ART for all HIV positive pregnant women), the new recommendation of the WHO is currently being implemented in place of Option B (ART only to HIV positive pregnant women with low CD_4 counts).

Table 1: Summary of the systematic review

	What the review authors searched for	What the review authors found
Studies	Randomized controlled trials (RCT)	Seven randomised controlled trials
Participants	HIV-infected, breastfeeding women and their infants	HIV-infected breastfeeding women and their infants
Interventions	Any antiretroviral therapy prophylaxis for breastfeeding mothers during breast-feeding. Any infant antiretroviral therapy prophylaxis during breastfeeding lasting more than four weeks.	All the 07 studies included were those that addressed maternal antiretroviral prophylaxis during breastfeeding (without infant extended prophylaxis), infant prophylaxis during breastfeeding, and both maternal and infant prophylaxis breastfeeding. Three studies evaluated maternal prophylaxis only; Five studies evaluated infant prophylaxis only; Once study evaluated both maternal and infant prophylaxis
Controls	Any controls	The following comparisons were made: • Triple ART prophylaxis during pregnancy and breastfeeding vs short ART prophylaxis before delivery. • Six months of breastfeeding with Zidovudine, Lamivudine and Lopinavir/Ritonavir vs Zidovudine, Lamivudine and Abacavir. • Single dose nevirapine vs six weeks of Zidovudine (infant). • Single dose Nevirapine vs six weeks of Nevirapine (infant). • Single dose Nevirapine and one week of Zidovudine vs control regimen and nevirapine for 14 weeks; or control regimen and dual prophylaxis for 14 weeks (infant). • Six weeks of Nevirapine versus six month of Nevirapine (infant). • Maternal triple ART vs infant Nevirapine or no intervention.
Outcomes	**Primary outcomes** **Maternal regimens** 1. HIV-free survival at six months and any other future time point among their children who were HIV-uninfected at 4-6 weeks of age. 2. HIV acquisition by 12 weeks, six months, 12 months, and 18 months among their children who were HIV-uninfected at 4-6 weeks of age. 3. Maternal severe adverse events including 4. hepatotoxicity in women given nevirapine with CD_4+ counts of 250-350 cells/mm **Infant regimens** 1. Mortality at six months, one year, two years and any other future time point among children who were HIV-uninfected at 4-6 weeks. 2. HIV-free survival at six months and any other future time point among children who were HIV-uninfected at 4-6 weeks of age. 3. Infant acquired antiretroviral resistance. 4. Infant severe adverse events (e.g., anaemia, neutropenia, other). **Secondary outcomes** **Maternal regimens** 1. Maternal mortality at one year, two years, and beyond. 2. Maternal response to subsequent antiretroviral therapy. 3. Maternal antiretroviral resistance. 4. Maternal adherence. 5. Child mortality at one and two years and any future time point. 6. Child response to subsequent antiretroviral therapy: clinical, virological, and immunological. **Infant regimens** 1. HIV acquisition by 12 weeks, six months, 12 months, and 18 months among children who were HIV-uninfected at 4-6 weeks of age. 2. Infant response to subsequent antiretroviral therapy: clinical, virological, and immunological.	The outcomes reported were: • Maternal adverse events • Maternal mortality • Maternal morbidity • Infant mortality • Infant morbidity • Resistance
Date of the most recent search: 14 January 2014.		
Limitations: This is a moderate quality systematic review**, AMSTAR =08/11**		
Citation: White AB, Mirjahangir JF, Horvath H, Anglemyer A, Read JS. Antiretroviral interventions for preventing breast milk trans-mission of HIV. Cochrane Database of Systematic Reviews 2014, Issue 10. Art. No.: CD011323. DOI: 10.1002/14651858.CD011323		

Table 2: Summary of findings

An extended Nevirapine regimen administered to infants for 14 weeks compared to single dose Nevirapine plus Zidovudine (1week)			
Patient or population: Breastfeeding infants of HIV-infected mothers **Settings:** Malawi (PEPI trial) **Intervention:** An extended Nevirapine regimen administered to infants for 14 weeks **Comparison:** Single dose of Nevirapine plus Zidovudine (1 week)			
Outcomes	**Relative effect (95% CI)**	**No of participants (studies)**	**Quality of evidence (GRADE)**
HIV Transmission at 24 months among those uninfected at birth Follow-up: 24 month	0.60 [0.46-0.78]	2019 (1)	moderate
An extended Zidovudine/Lamivudine/Lopinavir-Ritonavir regimen administered to mothers compared to short course Zidovudine (intrapartum Zidovudine, Retrovir/ Lamivudine/single dose of Nevirapine) for preventing breastfeeding transmission			
Patient or population: HIV-infected mothers and their breastfeeding infants **Settings:** Burkina Faso, Kenya, South Africa (Kesho Bora trial) **Intervention:** An extended Zidovudine / Lamivudine/ Lopinavir-Ritonavir regimen administered to mothers **Comparison:** Short course Zidovudine (intrapartum Zidovudine / Lamivudine/ single dose of Nevirapine			
Outcomes	**Relative effect (95% CI)**	**No of participants (studies)**	**Quality of evidence (GRADE)**
H IV transmission or Death at 12 months among those whose HIV diagnostic testing was negative at 6 weeks after birth Follow-up: 12 month	0.52 [0.28-0.93]	599 (1)	moderate
An extended Nevirapine regimen administered to infants for 6 weeks compared to single dose of Nevirapine for prevention of breastfeeding transmission			
Patient or population: Breastfeeding infants of HIV-infected mothers **Settings:** Ethiopia, India, Uganda (SWEN trial) **Intervention:** An extended Nevirapine regimen administered to infants for 6 weeks **Comparison:** single dose of Nevirapine			
Outcomes	**Relative effect (95% CI)**	**No of participants (studies)**	**Quality of evidence (GRADE)**
HIV Transmission or Death at 6 months among those whose HIV diagnostic testing was negative within 7 days of birth Follow-up: 6 month	0.72 [0.54-0.95]	1887 (1)	moderate

Applicability

In this review, two of the studies were conducted in South Africa, one in multiple sites in Ethiopia, India and Uganda, two in Malawi, one in Botswana, one study in multiple sites in Burkina Faso, Kenya, and South Africa, one study in in multiple sites in South Africa, Tanzania, Uganda and Zimbabwe. These findings may be applied in other low resources settings.

Conclusions

There is moderate quality evidence that provision of antiretroviral therapy either to the mother or to the child during breastfeeding may reduce the risk of HIV transmission to breastfeeding children.

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October 2014