Are antiretroviral drugs effective for preventing breast milk transmission of HIV

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. Without intervention, a significant proportion of children born to HIV-infected mothers acquire HIV through breastfeeding. Where alternatives to breast milk are available, it is recommended that HIV-infected mothers do not breastfeed. However, for a substantial number of HIV-infected women in the developing world, complete avoidance of breastfeeding is not practically possible or safe. Provision of antiretrovirals (ARVs) either to the mother or to the child during breastfeeding represents an intervention to reduce the risk of HIV transmission to breastfeeding children. In this review the authors explored the available evidence regarding the efficacy and safety of ARV prophylaxis regimens to reduce breast milk transmission of HIV.

Selection criteria and search methods
The authors selected randomized controlled trials (RCT) from January 1, 1994 to January 14, 2014 in which HIV-infected mothers breastfed their infants, and in which the mothers used antiretroviral prophylaxis while breastfeeding their children or their children received antiretroviral prophylaxis for at least four weeks while breastfeeding, were included.

Main results
Seven RCTs were included in the review. Several anti-retroviral drugs were compared and assessed for effectiveness and safety at follow up. They were used either singly or in combination with other agents. Some of the agents and combinations used were zidovudine, lamivudine, lopinavir/ritonavir, lamivudine / abacavir and nevirapine.

One trial compared single dose nevirapine plus one week zidovudine; the control regimen plus nevirapine up to 14 weeks; or the control regimen with dual prophylaxis up to 14 weeks. At 24 months, the extended nevirapine regimen group and the dual prophylaxis group had a lower risk of HIV transmission and of HIV transmission or death vs. the control. Evidence quality for outcomes in this trial was generally moderate to high. Another trial compared a maternal triple-drug antiretroviral regimen, infant nevirapine, or neither intervention. Infants in the maternal prophylaxis arm were at lower risk for HIV, and HIV infection or death when compared with the control group. Infants with extended prophylaxis had a lower risk of HIV infection and of HIV infection or death versus the control group infants. Evidence quality for outcomes in this trial was generally low to moderate.

A summary of the comparison between standard Nevirapine plus Zidovudine versus extended Nevirapine regimen is given in the table below.

Authors' conclusions
Antiretroviral prophylaxis, whether used by the HIV-infected mother or the HIV-exposed infant while breastfeeding, is efficacious in preventing mother-to-child transmission of HIV.
recommendation the world over is to start HAART when feasible in a pregnant woman. Standard recommendation is also to give a 6 week course of Zidovudine if the mother was not on HAART during pregnancy and shorter course of 4 weeks if the mother was on HAART. An ongoing trial (IMPAACT 1077BF) compares the efficacy and safety of maternal triple antiretroviral prophylaxis versus daily infant nevirapine for prevention of mother-to-child transmission through breastfeeding.

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Table: Summary of findings comparing Standard Nevirapine plus Zidovudine (Sd NVP) versus Extended Nevirapine

**Patient or population:** Breastfeeding infants of HIV-infected mothers

**Intervention:** An extended NVP regimen administered to infants for 14 weeks (oral dose of nevirapine (2mg/kg) once daily during week 2, then 4mg/kg once daily during weeks 3-14

**Comparison:** sdNVP plus ZDV (1week) - All infants received single oral dose of nevirapine (2mg/kg) plus oral zidovudine (4mg/kg) for 1 week. All mothers received intrapartum single dose nevirapine (except late presenters whose HIV infection was not identified until after they gave birth)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Quality of the evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV Transmission at 9 months among those whose HIV diagnostic testing was negative within 48 hours of birth</td>
<td>98 per 1000</td>
<td>56 per 1000 (41 to 75)</td>
</tr>
<tr>
<td>Infant Mortality at 9 months among those whose HIV diagnostic testing was negative within 48 hours of birth</td>
<td>71 per 1000</td>
<td>51 per 1000</td>
</tr>
<tr>
<td>HIV Transmission or Death at 9 months among those whose HIV diagnostic testing was negative within 48 hours of birth</td>
<td>168 per 1000</td>
<td>120 per 1000</td>
</tr>
<tr>
<td>HIV Transmission at 24 months among those uninfected at birth</td>
<td>156 per 1000</td>
<td>97 per 1000</td>
</tr>
<tr>
<td>Infant Mortality at 24 months among those uninfected at birth</td>
<td>165 per 1000</td>
<td>125 per 1000</td>
</tr>
<tr>
<td>HIV Transmission or death at 24 months among those uninfected at birth</td>
<td>242 per 1000</td>
<td>179 per 1000</td>
</tr>
</tbody>
</table>

Insanity – Doing the same thing over and over again and expecting different results. — Albert Einstein

Wise men talk because they have something to say; fools because they have to say something. — Plato

A family is a unit composed not only of children but of men, women, an occasional animal and the common cold. — Ogden Nash