Systematic review of the efficacy of antiretroviral therapies for reducing the risk of mother-to-child transmission of HIV infection

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CRD summary
This review found that zidovudine alone or combined with lamivudine and nevirapine monotherapy can prevent mother-to-child transmission of the human immunodeficiency virus. Different antiretroviral regimens are comparable in their ability to prevent transmission. The conclusions are likely to be reliable, but should be interpreted with some caution given the small number of included studies.

Authors’ objectives
To determine the efficacy of antiretroviral therapies in the reduction of mother-to-child transmission of human immunodeficiency virus (HIV) infection.

Searching
MEDLINE, EMBASE and the Cochrane Library were searched from inception to November 2006; the search terms were reported. Reference lists of relevant RCTs and reviews were screened to identify additional relevant studies. No language restrictions were applied.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies of antiretroviral therapy aimed at reducing the risk of mother-to-child transmission of HIV were eligible for inclusion. The included studies compared: zidovudine versus placebo or nevirapine; zidovudine plus nevirapine versus nevirapine; nevirapine plus zidovudine versus zidovudine with or without placebo; zidovudine plus lamivudine versus placebo; zidovudine plus lamivudine versus nevirapine; various regimens of zidovudine; nevirapine plus standard antiretroviral therapy versus placebo plus standard antiretroviral therapy; zidovudine for all women during the third trimester of pregnancy followed by a single dose of nevirapine versus placebo in mothers and infants. Full details of the dosages used were reported.

Participants included in the review
Inclusion criteria were not defined in terms of the participants but appear to have been pregnant women. The proportion of infants in the included studies who were breast-fed ranged from 0 to 99%. The studies were conducted in Europe, Africa, Thailand, and North and South America.

Outcomes assessed in the review
Studies had to report data on HIV infection in the infant, infant death (death of live born infant up to 12 months of age), stillbirth (no sign of life at birth), premature delivery (live born infant before 37 weeks' gestation) or low birth weight (<2,500 g) to be included in the review. The primary outcome was HIV infection in the infant.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Study quality was assessed in terms of randomisation, double-blinding, and withdrawals or drop-outs using the Jadad criteria. The studies were assigned a quality score out of a maximum of 5 points. The authors did not state how many reviewers performed the validity assessment.

Data extraction
One reviewer extracted the data onto a standardised form and a second reviewer checked the extraction. Any disagreements were resolved through discussion or by referral to a third reviewer. The definitions of HIV infection used by the primary study authors were accepted. Relative risks (RRs), risk differences (RDs) and numbers-needed-to-treat were calculated, together with their 95% confidence intervals (CIs), for each outcome for each study.

**Methods of synthesis**

How were the studies combined?
A random-effects model was used to pool RRs and RDs in the presence of significant heterogeneity.

How were differences between studies investigated?
Heterogeneity was assessed using the chi-squared statistic (significance level p<0.10).

**Results of the review**

Thirteen trials (11,843 women) were included in the review.

Three studies were unblended; all others were double-blinded. The quality scores ranged from 3 to 5.

Zidovudine versus placebo (5 studies): zidovudine significantly reduced the risk of mother-to-child transmission (pooled RR 0.57, 95% CI: 0.45, 0.71) and low birth weight (pooled RR 0.75, 95% CI: 0.57, 0.99). There were no significant effects of treatment on stillbirth, infant death or premature delivery.

Zidovudine plus lamivudine versus placebo (1 study): the antiretroviral treatment reduced the risk of infant HIV infection by 37% (95% CI: 10, 55). There were no significant effects of treatment on stillbirth or infant death.

Nevirapine plus zidovudine versus placebo plus zidovudine (1 study): the additional dose of nevirapine reduced the risk of mother-to-child HIV transmission by 68% (95% CI: 39, 83) and reduced the risk of death by 80% (95% CI: 10, 95). There was no effect on stillbirth, premature delivery or low birth weight.

Zidovudine versus nevirapine (1 study): nevirapine reduced the risk of mother-to-child transmission of HIV by 40% (95% CI: 13, 59). There were no differences between the treatments in terms of infant death, stillbirth and low birth weight.

Zidovudine for all women during the third trimester of pregnancy followed by a single dose of nevirapine versus placebo in mothers and infants (1 study): in the group receiving the single dose of nevirapine, the risk of mother-to-child transmission of HIV was reduced by 55% (95% CI: 19, 75).

The following treatment comparisons showed no differences in outcomes between intervention and comparison groups: zidovudine plus nevirapine versus nevirapine (2 studies); various regimens of zidovudine (1 study); zidovudine plus lamivudine versus nevirapine (1 study); nevirapine plus standard antiretroviral therapy versus placebo plus standard antiretroviral therapy (1 study).

**Authors’ conclusions**

Zidovudine alone or in combination with lamivudine, and monotherapy with nevirapine, can prevent mother-to-child transmission of HIV and may also reduce the risk of infant death. Different antiretroviral regimens are comparable in their ability to prevent mother-to-child transmission of HIV. The addition of a single dose of nevirapine to a zidovudine regimen for mothers and infants may further decrease the risk of transmission and infant death.

**CRD commentary**

This review addressed a focused objective that was supported by clearly defined inclusion criteria. The literature search was reasonable but did not include explicit attempts to locate unpublished studies, thus the review may be subject to publication bias. Study quality was assessed using published criteria. Appropriate steps were taken to minimise bias and errors in the data extraction, but it is unclear whether such steps were also taken at the study selection and quality assessment stages. Study details were reported clearly and extensively in the tables. The methods of analysis were appropriate for the data. The authors’ conclusions are likely to be reliable, but should be interpreted with some caution.
given the small number of included studies.

**Implications of the review for practice and research**

Practice: The authors did not state any implications for practice.

Research: The authors stated that further studies are required to assess the relative safety of the various antiretroviral regimens.

**Funding**

Not stated.

**Bibliographic details**


**PubMedID**

17489882

**DOI**

10.1111/j.1365-2710.2007.00825.x

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Anti-HIV Agents /therapeutic use; Antimetabolites /therapeutic use; Antiretroviral Therapy, Highly Active /methods; Child; Female; HIV Infections /drug therapy /virology; Humans; Infant; Infant, Newborn; Infectious Disease Transmission, Vertical /prevention & control; Lamivudine /therapeutic use; Nevirapine /therapeutic use; Pregnancy; Randomized Controlled Trials as Topic; Reverse Transcriptase Inhibitors /therapeutic use; Risk Factors; Treatment Outcome; Zidovudine /therapeutic use

**AccessionNumber**

12007001799

**Date bibliographic record published**

07/01/2008

**Date abstract record published**

01/09/2008

**Record Status**

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