Short course nevirapine was better than zidovudine for reducing the risk of mother to child transmission of HIV-1 infection

Jackson JB, Musoke P, Fleming T, *et al*. Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda: 18-month follow-up of the HIVNET 012 randomised trial. *Lancet* 2003;**362**:859–68.

Q In pregnant women with HIV-1 infection, is short course nevirapine more effective than a short zidovudine regimen for reducing the risk of mother to child transmission of HIV-1 infection?

METHODS

Design: randomised controlled trial.

Allocation: {concealed}†.*

Blinding: {unblinded}†.*

Follow up period: 6–8 weeks, 14–16 weeks, and 18 months.

Setting: {Mulago hospital in Kampala, Uganda}†.

Patients: 626 women who were {⩾18 years of age (mean age 24.5 y) at >32 weeks gestation, tested HIV-1 positive, and lived near the study site. Exclusion criteria included current antiretroviral or HIV-1 immunotherapy, uncontrolled hypertension, haemoglobin concentration <75 g/l, blood creatinine concentration >1.5 mg/dl, blood alanine aminotransferase concentration >3 times the upper limit of normal, and chronic alcohol or illicit drug use.}†

Interventions: Of the 313 mothers who were allocated to a 200 mg nevirapine tablet at the onset of labour, 308 gave birth to 308 firstborn neonates who received a single 2 mg/kg {calibrated oral syringe}† dose of nevirapine suspension 72 hours after birth or at discharge from the hospital. Of the 313 mothers who were allocated to two 300 mg zidovudine tablets at the onset of labour followed by a 300 mg tablet every 3 hours during labour, 311 gave birth to 311 firstborn neonates who received 4 mg/kg {calibrated oral syringe}† of zidovudine syrup twice daily for 7 days after birth. 99% of babies were breastfed.

Outcomes: HIV-1 infection and HIV-1 free survival in infants.

Patient follow up: 99%.

*See glossary.
†Guay LA, Musoke P, Fleming T, *et al*. *Lancet* 1999;**354**:795–802.

MAIN RESULTS

Analysis was by intention to treat. A third fewer babies who received nevirapine had HIV-1 infection or died with HIV-1 infection than did those who received zidovudine (table).

CONCLUSION

In pregnant women with HIV-1 infection, short course nevirapine was more effective than a short zidovudine regimen for reducing the risk of mother to child transmission of HIV-1 infection.

For correspondence: Dr J B Jackson, Johns Hopkins School of Medicine, Baltimore, MD, USA. bjackso@jhmi.edu

Source of funding: HIVNET; NIAID; NIH; DHHS and HPTN.

Commentary

The most effective strategy for reducing mother to child transmission of HIV will likely differ depending on the resources and practices of the setting. In less developed countries with limited resources, the preferred strategy would probably involve a short course therapy that is inexpensive and continues to be effective during breast feeding. Short course nevirapine has most of these attributes, and may even reduce the early transmission of HIV from breast milk.

In developed countries with resources to provide combination antiretroviral therapy (ART) for HIV infection and where bottle feeding is an acceptable alternative to breast feeding, short course nevirapine alone would not be routinely used because it is less effective for reducing mother to child transmission of HIV than longer course combination therapy. However, peripartum ART should be offered if a pregnant woman has not been on ART during pregnancy. The current US Public Health Service Task Force guidelines suggest 4 options: zidovudine, nevirapine, zidovudine plus lamivudine, and zidovudine plus nevirapine.[1]

The results of the study by Jackson *et al* suggest that in the setting where peripartum ART is recommended, short course zidovudine alone would be less effective for reducing mother to child transmission of HIV. When choosing an intervention, the short term and long term adverse effects on both the mother and baby need to be considered. In this study, the short term toxicity for both mother and baby was low, and little difference existed between the 2 groups. Furthermore, fulminant hepatitis and Stevens Johnson syndrome, which have previously been reported with nevirapine, did not occur in this study. Long term toxicity in infants is not yet known. However, short exposure peripartum is unlikely to cause developmental abnormalities compared with exposure earlier in gestation. A potential long term problem for mothers is the development of resistance to nevirapine. This does occur but appears to be transient. It is, however, unclear how this will affect a mother's response to combination treatment with nevirapine or other non-nucleoside reverse transcriptase inhibitors given later.

Susan King, MD
Hospital for Sick Children and University of Toronto
Toronto, Ontario, Canada

1 Public Health Service Task Force recommendations for the use of antiretroviral drugs in pregnant women infected with HIV-1 for maternal health and for reducing perinatal HIV-1 transmission in the United States. *MMWR Recomm Rep* 1998;*47*(No RR-2):1–30.

Nevirapine (Nev) *v* zidovudine (Zid) for reducing the risk of mother to child transmission of HIV-1 infection*

Outcomes	Nev	Zid	RRR (95% CI)	NNT (CI)
HIV-1 infection				
6–8 weeks	11.8%	20%	39% (12 to 59)	13 (9 to 43)
18 months	15.7%	25.8%	37% (14 to 55)	11 (7 to 28)
HIV-1 infection or death				
18 months	20.7%	30.7%	33% (11 to 49)	10 (7 to 30)

*Abbreviations defined in glossary; RRR, NNT, and CI calculated from data in article.