



Single-dose Perinatal Nevirapine plus standard Zidovudine to prevent mother-to-child transmission of HIV-1 in Thailand.

CITATION:

Lallemant M, Jourdain G, Le Coeur S, et al. for the Perinatal HIV Prevention Trial. Single-dose Perinatal Nevirapine plus standard Zidovudine to prevent mother-to-child transmission of HIV-1 in Thailand. *The New England Journal of Medicine* 2004; 351(3): 217-28.

RESEARCH QUESTION:

Does a single-dose of Nevirapine, administered perinatally, in addition to standard Zidovudine prophylaxis prevent mother-to-child transmission of HIV-1 in Thailand?

THE STUDY

Randomised, double-blind trial of three treatment regimens.

STUDY SETTING

HIV-1 positive pregnant Thai women, who were presently being treated with Zidovudine prophylaxis (during their third trimester of pregnancy). Multi-centre trial (37 sites in Thailand). Participants recruited between January 15th 2001 until February 28th, 2003. Ethics approval granted by the ethics committee of the Thai Ministry of Public Health, Chiang Mai University and the Harvard School of Public Health.

PARTICIPANTS

Included:

HIV-1 positive pregnant women participating in the national program of voluntary counselling and testing who were receiving Zidovudine prophylaxis (starting at 28 weeks gestation or as soon as possible thereafter) at any of the 37 study sites in Thailand.

The patients must have received Zidovudine for at least two weeks, signed informed consent, agreed not to breast feed, and lab values of:

haemoglobin > 8.0g/dl; absolute neutrophil count > 750 cells/mm³ ; alanine aminotransferase level < 35 U/l; creatine level < 1.5mg/dl.

Excluded:

Maternal of fetal condition; concomittant treatment that contraindicated treatment with Zidovudine or Nevirapine, oligohydramnois; unexplained polyhydramnois or in utero anaemia; medical condition that required immediate use of highly active antiretroviral therapy.

INTERVENTION

Standard Zidovudine prophylaxis treatment regime:

All women received 300mg Zidovudine twice daily starting at 28 weeks gestation or as soon as possible thereafter. The dosing regime was changed to 300mg every three hours from the onset of labour until delivery. Infants received 2mg of Zidovudine per kilogram body weight in an oral suspension every six hours for one week after birth. In accordance with national guidelines, if the mother had received Zidovudine for a period of less than 4 weeks, the infant was treated for 4 to 6 weeks after birth.

Nevirapine-Nevirapine group: standard Zidovudine prophylaxis + single oral dose of Nevirapine (200mg) at onset of labour and baby received Nevirapine oral suspension 6mg fixed dose) between 48 and 72 hours after birth.

Nevirapine-Placebo group: standard Zidovudine prophylaxis + single oral dose of Nevirapine (200mg) at onset of labour and baby receives placebo between 48 and 72 hours after birth.

Placebo-Placebo group: standard Zidovudine prophylaxis + placebo at onset of labour and baby receives placebo between 48 and 72 hours after birth.

OUTCOMES

Primary: Infection with HIV in infants (positive PCR test in blood samples obtained on two separate occasions, after 1 month of age). Adverse events. Safety and efficacy of Nevirapine administered perinatally together with standard Zidovudine prophylaxis.

Secondary: Evaluate the effect of the administration of perinatal Nevirapine to newborns (N-N group vs N-P group in final analysis).

RISK OF BIAS (Risk Scale: Low – Moderate – High)

SELECTION BIAS: Low

Study drugs were identified by random numbers with the use of permuted blocks of six in a ration of 1:1:1. Women were randomly assigned to groups. No mention of allocation concealment. Baseline characteristics of women, deliveries and the newborn were similar across groups.

PERFORMANCE BIAS: Low

It appeared that both the patient and the provider were blinded to the treatment being provided.

DETECTION BIAS: Low-moderate

Safety assessment was conducted by persons blinded to treatment assignment. Not clear whether or not other assessors were blinded.

ATTRITION BIAS: Low

A similar number of individuals (~10%) were lost to follow-up/still birth or unable to be evaluated from the three treatments. An “as-randomised analysis and pre-protocol analysis was performed”.

STUDY FINDINGS:

	Treatment	Event Rate	RRR	ARR	NNT
First Interim	NN	1.1%	82%	0.051	20
	PP	6.3%	32%;100%	0.024;0.078	13;42
Analysis	NN	1.1%	45%	0.009	111
	NP	2.1%	-46%;100%	-0.009;0.027	
	NP	2.1%	68%	0.042	24
	PP	6.3%	21%;100%	0.013;0.071	14;77
Final Analysis	NN	2.0%	26%	0.007	143
	NP	2.8%	-33%;85%	-0.009;0.023	

ADVERSE EVENTS

Mother: No severe rashes observed. At day 10, mild rashes were observed in 3.8 percent of mothers. Rates of serious adverse events similar across the groups – relating to pregnancy = 59%, infection or HIV = 26%, possibly Zidovudine prophylaxis (i.e. anaemia) = 7%, possibly Nevirapine (allergic reaction during therapy) = 7% out of total 216 total reported incidents.

Child: Rashes observed in 15.9% and 7.5% of babies at day 10 and 45 post birth. No significant differences between treatment groups. Neonatal or obstetrical = 11%, congenital abnormalities = 6%, infection, including HIV = 72%, possibly Zidovudine (i.e. anaemia) = 2% and other causes = 9% of 598 total reports of adverse effects.

COMMENTS

Good quality trial. Single-dose perinatal Nevirapine plus standard Zidovudine reduce mother-to-child transmission of HIV.

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Date: 25 January 2005