A phase I/II study of the safety and pharmacokinetics of nevirapine in HIV-1-infected pregnant Ugandan women and their neonates (HIVNET 006)

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Objective: To determine the safety, pharmacokinetics, tolerance, antiretroviral activity, and infant HIV infection status after giving a single dose of nevirapine to HIV-1-infected pregnant women during labor and their newborns during the first week of life.

Design: An open label phase I/II study.

Setting: Tertiary care hospital, Kampala, Uganda.

Patients and interventions: Nevirapine, 200 mg, was given as a single dose during labor to 21 HIV-1-infected pregnant Ugandan women. In cohort 1, eight infants did not receive nevirapine whereas in cohort 2, 13 infants received a single dose of nevirapine, 2 mg/kg, at 72 h of age.

Outcomes: The number and type of adverse events; nevirapine concentrations in the plasma and breast milk; maternal plasma HIV-1 RNA copy number before and up to 6 weeks after delivery; and HIV-1 infection status of the infants were monitored.

Results: Nevirapine was well tolerated by women and infants; no serious adverse events that were related to nevirapine were observed. Median nevirapine concentration in the women at delivery was 1623 ng/ml (range 238–2356 ng/ml); median cord/maternal blood ratio of 0.75 (0.37–0.93). The median half-life in women was 61.3 h (27–90 h) and the transplacental nevirapine half-life in infants who did not receive a neonatal dose was 54 h. The median half-life after a single dose at 72 h in infants was 46.5 h. During the first week of life, the median colostrum/breast milk to maternal plasma nevirapine concentration was 60.5% (25–122%). The median nevirapine concentration in breast milk 1 week after delivery was 103 ng/ml (25–309 ng/ml). Plasma nevirapine concentrations were

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Sponsorship: This trial was sponsored by the HIV Network for Prevention Trials, Division of AIDS, NIAID/NIH contract no. N01-AI-35173 and subcontract no. AI-35173-121.

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Date of receipt: 6 October 1998; revised: 30 November 1998; accepted: 7 December 1998.

above 100 ng/ml in all infants from both cohorts tested at age 7 days. Maternal HIV-1 RNA levels decreased by a median of 1.3 logs at 1 week postpartum, and returned to baseline by 6 weeks postpartum. Detectable plasma HIV-1 RNA was observed in one out of 22 (4.5%) infants at birth; three out of 21 (14%) at 6 weeks; and four out of 21 (19%) at 6 months of age.

Conclusion: The administration of a single dose of nevirapine to women during labor and to their newborns at 72 h was well tolerated and showed potent antiretroviral activity in the women at 1 week after dosing without rebound above baseline 6 weeks after a single dose. The nevirapine concentration was maintained above the target of 100 ng/ml in infants at age 7 days, even in those infants not receiving a neonatal dose. This regimen has promise as prophylaxis against intrapartum and early breast milk transmission in a breastfeeding population.

AIDS 1999, **13**:479–486

Keywords: HIV vertical transmission, nevirapine, pharmacokinetics, Uganda

Introduction

The transmission of HIV-1 from an infected mother to her infant is estimated to be 15–40% in various developed and developing countries, with more than half of the transmission probably occurring late in pregnancy or during labor and delivery [1,2]. Results of the Pediatric AIDS Clinical Trials Group Protocol (PACTG 076) showed that a regimen of azidothymidine (AZT) starting early in pregnancy, administered intravenously during labor and delivery, and orally to neonates for the first 6 weeks of life reduced the rate of HIV-1 vertical transmission by two-thirds [3]. Virological data from this trial showed that there was poor correlation between the decrease in maternal plasma HIV-1 RNA levels and vertical transmission, suggesting that the efficacy of the regimen may be caused by antiretroviral prophylaxis of the neonate at the time of exposure at birth [4]. If this is the case, the provision of antiretroviral therapy covering the peripartum period alone may be sufficient to reduce vertical transmission and offer an affordable and feasible regimen for HIV-1-infected pregnant women in developing countries.

Nevirapine (a non-nucleoside reverse transcriptase inhibitor) is an excellent candidate for a single-dose antiretroviral intervention administered during labor because of its potent antiviral effect (an IC_{50} of 10 ng/ml), rapid oral absorption, good bioavailability, long half-life (46 h at 200 mg/day in adults), and ability to cross the placenta [5–8]. Therefore, a phase I/II trial was undertaken to determine the maternal and neonatal pharmacokinetics and short-term safety and tolerance of a single dose of nevirapine, given to HIV-1-infected pregnant Ugandan women during labor and a single neonatal dose of nevirapine during the first week of life. Because there are no in-vivo data on the effect of nevirapine on HIV-1 subtypes A and D, the predominant HIV-1 subtypes in Uganda [9], the magnitude of decrease in HIV-1 plasma RNA levels in pregnant women after a single dose of nevirapine in labor was also determined. In addition, because nearly all mothers breastfeed in Uganda, the penetration of nevirapine into colostrum/early breast milk was also evaluated, and nevirapine levels in plasma were correlated with those in breastmilk. The HIV-1 infection status of the infants at birth, 6 weeks, and 6 months of age was also determined.

Methods

Regimen

The study was a sequential two-arm phase I/II open label study, in which eight HIV-1-infected pregnant Ugandan women received a single 200 mg tablet of nevirapine upon presentation to the hospital in active labor. After this first cohort of mothers had delivered their infants, a second cohort was enrolled in which an additional 13 HIV-1-infected pregnant Ugandan women received a single 200 mg tablet of nevirapine in labor and their neonates received a single oral dose of nevirapine (2 mg/kg) at 72 h of age. The target nevirapine plasma level in the infant one week after delivery was 100 ng/ml or higher. This target was chosen because it is 10 times greater than the nevirapine IC_{50} for HIV-1.

Study population

Women in the general antenatal clinics at Mulago Hospital in Kampala, Uganda, received voluntary counselling, and those accepting HIV-1 testing were screened for HIV-1 infection by enzyme immunoassay (EIA) for HIV-1 antibody. Women were eligible for the study if they were 34 weeks' gestation or over, were Western blot positive for HIV-1 antibody, had no

evidence of clinically significant medical or HIV-1-related illness, lived within 15 km of Mulago Hospital, and were receiving no other antiretroviral or HIV immunotherapy. Exclusion criteria included a hemoglobin level of less than 7.5 g/dl, a blood creatinine level greater than 2.0 mg/dl, a blood alanine aminotransferase level over five times the upper limit of normal, a congenital anomaly incompatible with life by ultrasound, and receipt of the following medications within 2 weeks of enrollment: benzodiazepines, anticoagulant therapy, augmentin, phenobarbital, or anticonvulsants. The trial was approved by the Institutional Review Boards of Johns Hopkins University, Makerere University, and Mulago Hospital. Women enrolled in the trial gave informed consent.

Study procedure

Enrolled women were instructed to report to the labor ward at the first signs of labor. They were given a single 200 mg nevirapine tablet when in active labor, as defined by a dilated cervix greater than 4 cm. The progress of labor and delivery were closely monitored. At delivery, maternal and cord bloods were obtained. Infant bloods were drawn at specific timepoints during the first week of life (see pharmacokinetics section). Consequently, the majority of mothers and their infants remained hospitalized for 1 week after delivery to ensure that the scheduled blood samples were not missed. Mothers and infants were seen in the Mother Child Research Clinic for follow-up. The mothers were evaluated at 6 weeks after delivery and the infants at 6 weeks, 6 and 18 months of age.

Safety and toxicity

The study included careful toxicity monitoring of the mother and infant from the onset of labor through the first week after delivery. Clinical evaluation and laboratory monitoring of maternal and neonatal complete blood counts, serum alanine aminotransferase, bilirubin and creatinine levels were performed.

Pharmacokinetics

Plasma samples for nevirapine concentration were drawn from study mothers at 0, 1, 2, 3, 4, 6, 8, 12, 24, 48, 72, and 168 h after dosing. Colostrum/breast milk samples were collected at 48, 72, and 168 h after dosing and was frozen as whole breast milk at −70°C. Eight neonates born to study women in cohort 1 received no nevirapine after birth. Plasma samples taken from the infants for nevirapine concentration were obtained from cord blood and at 24, 48, 72 and 168 h after birth. Thirteen of 14 neonates born to 13 study women (one set of twins) in cohort 2 received a single 2 mg/kg dose of an oral nevirapine suspension 72 h after birth. One of the 14 infants died within 24 h of delivery and therefore did not receive the drug. Plasma samples for nevirapine assay were obtained from cord blood and at 24, 48, 72 (trough before infant dose), 96, 108, 120, and 168 h after birth. Nevirapine concentrations in the plasma and colostrum/breast milk were determined by high pressure liquid chromatography [10].

Pharmacokinetic analysis was performed using non-compartmental methods, as previously described [10]. For the study mothers, peak concentration (C_{max}), time of peak concentration (T_{max}), elimination half-life ($t_{1/2}$), area under the concentration time curve from time 0 and extrapolated to infinity (AUC), oral clearance (Cl/F), and steady state volume of distribution (V_{ss}/F) were determined. The median percentage of AUC estimated by extrapolation was 9.9%. For the infants not receiving a postnatal dose, C_{max}, T_{max}, washout $t_{1/2}$ (from 4 h to 7 days after birth), and the ratio of nevirapine concentration in the cord blood to that of the maternal plasma at delivery were determined. For the infants receiving a postnatal dose, washout $t_{1/2}$ was calculated up to the time of infant dosing and $t_{1/2}$ after the dose was calculated. Pharmacokinetic calculations were performed using two commercial personal computer programs (RSTRIP, Micromath Scientific Software, Salt Lake City, UT, USA and Microsoft Excel, Seattle, WA, USA).

Diagnosis of infant HIV infection

Plasma from infants was tested at birth, 6 weeks, and 6 months of age for the detection of HIV-1 RNA using the qualitative Roche AMPLICOR MONITOR assay (Roche Diagnostics, Branchburg, NJ, USA) with an additional set of primers (SK 151–145) in order to detect all HIV-1 subtypes. Infants were considered to be HIV-1 infected if they had detectable HIV RNA on two separate blood draws, or a reactive EIA (HIV type 1 Vironostika Organon-Teknika, Durham, NC, USA) and confirmed by Western blot (Cambridge BioTech Corporation, Worcester, MA, USA) for HIV-1 antibody at 18 months of age. Infants who had a single positive plasma HIV-1 RNA test were considered to have probable infection. Where possible, HIV culture using the National Institute of Allergy and Infectious Disease (NIAID) AIDS Clinical Trials Group procedure was also performed to confirm the HIV-1 infection in the infants [11].

Statistical analysis

The medians of pharmacokinetic parameters, log HIV-1 RNA levels and log HIV-1 RNA changes from baselines were obtained. Log_{10} of RNA plasma levels (after adding a constant of 0.1 in order to avoid log (0) values) were taken in order to obtain an approximate normal distribution of the values. Approximate 95% confidence intervals of medians were obtained using bootstrap resampling methods. In addition to the confidence intervals for changes in HIV-1 RNA levels from baseline, levels were evaluated for statistical significance using the exact Wilcoxon signed rank test with continuity correction testing for H_A:mu = 0 for RNA differences.

Results

A total of 30 pregnant women were enrolled in the sequential phase I study (11 in cohort 1 and 19 in cohort 2). Nine women, however, delivered before nevirapine could be administered and two women received the drug within 30 min of delivery. In women who did receive the drug, the median lag time from maternal dosing in labor to delivery was 3.8 h and in 80% of women this was over 2 h. The median maternal CD4 cell count at baseline in the 21 women who received nevirapine was 595 cells/μl (range 207–1428 cells/μl) with a median baseline plasma HIV RNA level of 22 746 (<400–1 796 670) copies per ml. Eight infants were born to the eight mothers who received nevirapine in cohort 1, and 14 infants (one set of twins) were born to 13 mothers who received nevirapine in cohort 2. Thirteen infants in cohort 2 received the 2 mg/kg dose of nevirapine at 72 h after birth. One infant died within 24 h of delivery from sepsis and respiratory distress, and therefore did not receive the study drug. Pharmacokinetic sampling on the mother terminated at that time, and this mother–infant pair was excluded from the pharmacokinetic analysis.

Maternal pharmacokinetics

Table 1 and Fig. 1 summarize the maternal pharmacokinetic data in 20 evaluable mothers. The median maternal plasma nevirapine concentration at delivery was 1644 ng/ml (range 238–2356 ng/ml) and a median cord/maternal blood ratio was 0.75 (range 0.37–0.93) (Table 2). The median half-life of nevirapine in the mothers was 61.3 h (range 27.4–90 h). The median ratio of breast milk to maternal nevirapine concentration was 60.5% (range 25.3–122.2%). Breast milk nevirapine concentration declined during the first week of life from a median of 454 ng/ml (range 219–972 ng/ml) at 48 h after birth to 103 ng/ml (range 25–309 ng/ml) at 7 days, in parallel with the decline in maternal plasma nevirapine concentration.

Infant pharmacokinetics

Table 2 and Fig. 2 summarize the infant pharmacokinetic data in cohort 1. One cohort 1 infant was born less than 30 min after maternal nevirapine dosing, and this infant's cord blood sample was not drawn. This infant has been excluded from the data analysis. The other seven cohort 1 infants were born two or more hours after maternal dosing (median 3.8 h), and cord blood nevirapine concentrations exceeded the 100 ng/ml target concentration in all infants (median concentration is 1175 ng/ml). Median washout $t_{1/2}$ was 50 h and the median concentration at 7 days of life was 220 ng/ml, with a range of 109 ng/ml to 292 ng/ml.

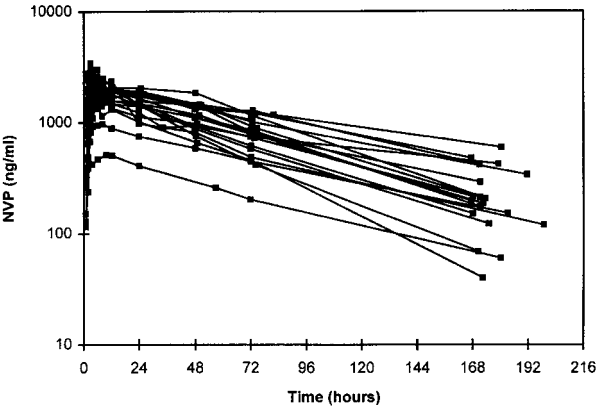

Fig. 1. Cohort 1 and 2 mothers: maternal nevirapine pharmacokinetics after a single dose of 200 mg nevirapine given during active labor (n = 20).

Table 2 and Fig. 3 summarize the infant pharmacokinetic data in cohort 2. One cohort 2 infant was born 30 min after maternal dosing with a cord blood concentration of 77 ng/ml. The other 12 cohort 2 infants were born at least 1 h after maternal dosing (median 4 h), and the cord blood concentration exceeded the 100 ng/ml target concentration in all (median 1122 ng/ml). Median nevirapine just before the day 3 infant dose was 595 ng/ml. One infant who was born 1 h after maternal dosing had a cord blood nevirapine concentration of 137 ng/ml, which declined to a day 3 pre-dose concentration of 77 ng/ml. The day 3 pre-dose concentration exceeded 100 ng/ml in the other infants. Median washout $t_{1/2}$ of transplacentally acquired nevirapine was 72.1 h, and $t_{1/2}$ after the

Table 1. Maternal nevirapine pharmacokinetic data after a single oral 200 mg dose (n = 20)

Pharmacokinetic parameters	Median (range)	95% CI
Time to delivery after dosing (h)	3.8 (0.4–12.3)	2.9–6.4
NVP conc. at delivery (ng/ml)	1644 (238–2356)	1606–1958
C_{max} (ng/ml)	2032 (515–3457)	1722–2273
T_{max} (h)	7.1 (2.0–26.1)	4.0–8.6
AUC (ng/h/ml) extrapolated	163 300 (43 790–268 300)	133 953–180 189
Clearance F (l/h)	1.23 (0.75–4.57)	1.11–1.50
Clearance F (ml/kg/h)	20.36 (12.44–63.43)	17.59–26.38
Vd/F (l/kg)	1.54 (0.66–4.49)	1.19–1.71
Terminal $t_{1/2}$ (h)	61.3 (27.4–90.4)	50.6–64.3
Weights (kg)	61.5 (48.2–72.0)	57.8–64.9

AUC, area under the concentration time curve; NVP, nevirapine.

Table 2. Infant nevirapine pharmacokinetic data in cohorts 1 and 2

Pharmacokinetic parameters	Median (range)	95% CI
Cohort 1 (maternal dosing only) (n = 7)		
Cord blood concentration (ng/ml)	1175 (691–1887)	826–1384
Cord/maternal ratio	80% (37–92%)	50.9–81.0
C_{max} (ng/ml) – washout	1605 (1046–1996)	1269–1720
T_{max} (h after birth) – washout	0 (0–28.6)	0.0–25.1
Terminal $t_{1/2}$ (h) – washout	50.0 (39.8–85.1)	45.2–66.3
Concentration at age 7 days (ng/ml)	220 (109–292)	178–280
Cohort 2 (maternal and infant dosing) (n = 13)		
Cord blood concentration (ng/ml)	1122 (77–1977)	347–1354
Cord/maternal ratio	72.9% (57.6–93.0%)	69.8–81.6
Pre-dose concentration (ng/ml)	595 (77–1224)	284–662
C_{max} (ng/ml) – post-dose	1279 (736–2120)	938–1368
T_{max} (h after birth)	24.6 (22.0–38.3)	23.4–25.4
Terminal $t_{1/2}$ (h) – washout	72.1 (36.6–84.3)	42.2–75.8
Terminal $t_{1/2}$ (h) – post-dose	46.5 (23.6–81.6)	31.7–54.7
Concentration at age 7 days (ng/ml)	383 (171–757)	282–444

administered dose decreased in all infants (median 46.5 h, $P = 0.0006$ compared with washout $t_{1/2}$, paired *t*-test). The nevirapine concentration at 7 days of life exceeded the 100 ng/ml target in all infants (median 383 ng/ml).

Plasma HIV-1 RNA levels

Of the 19 women with a 7 day HIV-1 RNA level available, there was a median 1.3 (95% CI −1.46, −1.17) log reduction in maternal plasma RNA levels 7 days after the single dose of nevirapine. The median maternal plasma RNA level at 6 weeks was not significantly different than that at baseline (16 707 versus 22 746 copies/ml, $P = 0.7$). The majority of plasma RNA levels had returned to baseline by 6 weeks after the receipt of nevirapine. The maternal HIV-1 RNA levels at delivery among the four HIV transmitting women were 304290; 291392, 672, and 556 copies per ml; the median maternal HIV-1 RNA levels at delivery in the 17 women who did not transmit to their infant was 29 307 copies per ml (range < 400–1 796 670 copies/ml).

Infant HIV infection status

At birth, one (4.5%) of 22 infants was HIV-1 infected. One infant, who tested negative, died the day after birth leaving 21 evaluable infants for subsequent testing. At 6 months of age four (19%) of 21 infants were HIV-1 infected (one in cohort 1 and three in cohort 2). One of the four HIV-infected infants was initially positive for plasma HIV RNA at birth, two were initially HIV RNA positive at 6 weeks of age, and one was initially HIV RNA positive at 6 months of age. Two of the infants with positive plasma HIV RNA tests (one positive at birth and the other positive at 6 weeks of age) also had a confirmatory positive HIV culture; one infant had a confirmatory HIV RNA test. One of these four infants had a single positive plasma HIV RNA test, but died before a confirmatory test and was therefore considered as probably HIV-1 infected.

Safety and tolerance

There were no serious adverse events or grade 3 or 4 clinical or laboratory toxicities thought by investigators to be related to nevirapine among the mothers of either

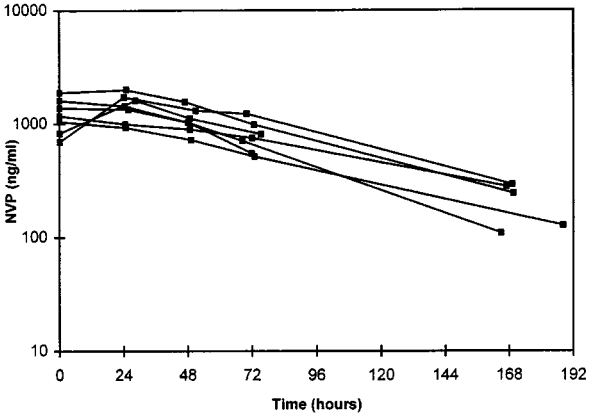

Fig. 2. Cohort 1: infant nevirapine pharmacokinetics after a single oral maternal nevirapine dose of 200 mg in labor (n = 7).

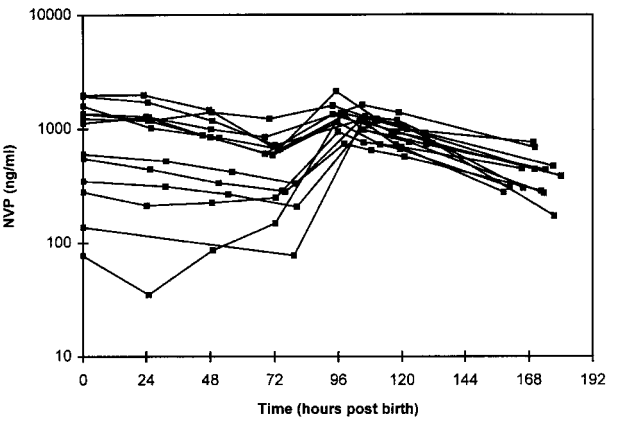

Fig. 3. Cohort 2: infant nevirapine pharmacokinetics after a single oral maternal nevirapine dose of 200 mg in labor and infant dosing of 2 mg/kg of nevirapine at 72 h of life (n = 13).

cohort. There were five serious adverse events including two deaths in the infants in cohort 1. Only one of the five serious adverse events was thought by the investigators to be possibly, but not likely, study drug related. This infant developed respiratory distress at birth and seizures after a difficult and prolonged labor requiring the use of forceps. In cohort 2 there were seven serious adverse events, including two infant deaths, although none were related to the study drug.

Discussion

This phase I/II study was primarily carried out to evaluate the safety, toxicity, and pharmacokinetics of nevirapine administered to HIV-1-infected pregnant Ugandan women in labor and their neonates in the first week of life. The study showed that a single maternal dose given in labor and a single dose to the infant at 72 h of life was well tolerated in both mothers and infants, and did not result in any serious adverse events likely to be related to nevirapine. There were no serious skin rashes, abnormal complete blood counts, or elevations of liver function tests or creatinine associated with the use of nevirapine in this study.

Pharmacokinetic data revealed that a single oral 200 mg dose of nevirapine given to the mother in labor at least 1 h before delivery maintains a nevirapine plasma concentration above the targeted 100 ng/ml in both the mother and the infant 7 days after birth. The addition of a single infant oral dose of 2 mg/kg of nevirapine at 72 h of life was well tolerated and maintained nevirapine levels over 170 ng/ml 7 days after birth. Nevirapine appeared to be rapidly absorbed and transferred across the placenta within 1 h after oral ingestion. Concentrations of nevirapine in cord blood were between 17 and 58 times the IC_{50} of nevirapine in infants whose mothers received nevirapine more than 1 h before delivery.

Nevirapine elimination was prolonged in the study mothers and infants, with considerable interpatient variability. In the mothers, the median half-life of nevirapine was 61.3 h, with a range of 27.4–90.4 h. By comparison, nevirapine half-life after an initial single dose averages 40 h in non-pregnant adults [8,12]. The primary elimination pathway for nevirapine appears to be hepatic oxidative metabolism by cytochrome p450 enzymes of the CYP3A family, although CYP2B6 enzymes also contribute [13]. It is not clear if the prolonged elimination of nevirapine in the study mothers during and immediately after labor was caused by changes associated with labor or by decreased hepatic enzyme metabolic activity associated with pregnancy.

In the study infants, the median half-life of transplacentally acquired drug (washout) for both cohorts combined was 54.0 h, with a range of 36.6–85.1 h. In the cohort 2 infants, median half-life after the dose administered at 72 h of age was 46.5 h; less than the washout half-life in every cohort 2 infant. The acceleration of nevirapine elimination during the first week of life may be caused by normal changes in hepatic blood flow and enzyme activity seen after birth or by autoinduction of cytochrome P450 enzymes by nevirapine. In older infants and children, nevirapine elimination is relatively fast, with a mean half-life of 30.6 h [14].The relatively slow elimination of nevirapine in the newborns in our study conforms to the pattern previously described for CYP3A4 activity in infants and children – initially low in newborns, increasing to adult levels by 6–12 months of life, exceeding adult levels during years 1–4, then declining to adult levels by the end of puberty [15].

Nevirapine levels in breast milk were maintained above 100 ng/ml in most of the mothers throughout the first week after delivery. Assuming a daily intake of 80 ml/kg of breast milk on day 2 and 180 ml on day 7, the amount of nevirapine provided to the infant via breast milk was small, ranging from a median of 0.06 mg/kg on day 2 to 0.02 mg/kg on day 7. Nevirapine has, however, been shown to penetrate cell-free virions and inactivate virion-associated reverse transcriptase *in situ* [16]. Therefore, the presence of nevirapine in breast milk at therapeutic concentrations has the potential to offer some protection against breast milk transmission of HIV-1.

In the study, mothers were not given nevirapine until they presented to the hospital in labor, in order to obtain accurate pharmacokinetic data and monitor for adverse reactions. Consequently, nine women (30%) delivered at home or on their way to the hospital before nevirapine could be given. Any labor regimen, if shown to be efficacious in preventing vertical transmission, would be more effective if women were given a dose to take home with them, so that they could take nevirapine at the onset of labor pains. It would also seem prudent in a phase III trial to give the infant the oral dose of nevirapine as soon as possible after delivery if the mother delivered less than an hour after dosing, because the cord blood of the two infants in this study who were born within half an hour after maternal dosing had less than 100 ng/ml of nevirapine.

The antiviral activity of nevirapine appeared to be quite strong, resulting in a relatively consistent median 1.3 log reduction in maternal plasma HIV RNA at 1 week after a single 200 mg dose in all mothers. As HIV-1 RNA levels were not measured after 7 days until 6 weeks after delivery, there could have been a further reduction because nevirapine levels were still well above the IC_{50} in most women at 7 days. By

6 weeks after delivery, there was no significant change in maternal plasma HIV-1 RNA levels from baseline levels. The presence of the codons Y181 and Y188 mutations associated with nevirapine resistance were not tested for in any of these mothers 6 weeks after delivery. Maternal plasma HIV-1 RNA levels were also not significantly different at delivery from baseline, as might be expected considering the short amount of time between dosing and delivery and the life cycle of the virus. Therefore, if nevirapine turns out to be efficacious in preventing vertical transmission at the time of delivery, it is unlikely to be caused by a reduction in maternal viral load. The decrease in viral load during colostrum feeding might, however, impact on postnatal transmission.

Although we did not subtype the virus of these mothers, previous subtyping of HIV in Uganda shows that approximately 45% of infected individuals have subtype A, 35% subtype D, 5 % subtype C, and 15% subtypes A and D (dual infection or recombinant) [9]. Assuming that this distribution of subtypes is similar in our study population, nevirapine appears to have a potent antiviral effect against HIV-1 subtypes other than subtype B.

Because the majority of HIV-1 vertical transmission is thought to occur around the time of delivery, this simple regimen could be very effective in substantially reducing the vertical transmission rate in this population. The 19% transmission rate in this study at 6 months of age, although lower than the historical transmission rate of 26% observed previously in this population [17], cannot be compared because of the problematical nature of using historical controls and the small numbers involved in this phase I/II study.

Nevertheless, these data verify that maternal treatment with a single dose of nevirapine during labor will result in sustained and potent nevirapine levels in the neonate and mother at the time of exposure to HIV-1 during delivery and immediately postpartum through the colostrum. Theoretically, this regimen has the potential to prophylax the neonate against the risk of maternal–infant HIV-1 transmission if exposure occurs primarily at the time of delivery. Such a regimen, if efficacious, would also be simple, inexpensive, and applicable, especially in the setting of developing countries.

Acknowledgements

The investigators wish to thank and acknowledge Marguerite Ro, Estelle Piwowar-Manning, Jana Parsons, Sam Kabengera, and Julius Onencan for laboratory technical support; Lynda Emel for data monitoring support; Lois Rowland from Boehringer-Ingleheim for the measurement of nevirapine concentrations; Joyce Nakakande, Agnes Sendege, Bihira Mediatrix, Mary Kasango, Grace Manyangwa for nursing support; and Edith Kibuuka, Joyce Matovu, Godfrey Sempa, and Jessica Lukandwa for counselling support; the midwives in labor suite 6D/E of New Mulago Hospital; and Maureen Myers of Boehringer-Ingleheim for her staunch support and the provision of nevirapine. The content of this publication does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the United States government.

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