Operational effectiveness of single-dose nevirapine in preventing mother-to-child transmission of HIV

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Objective To determine the operational effectiveness of the South African programme for preventing mother-to-child transmission (PMTCT) of HIV in reducing rates of early transmission of infection.

Methods Participants were mother–infant pairs who participated in the South African PMTCT programme between October 2002 and November 2004. This was a prospective cohort study. Three sites in different provinces were selected to represent differences in socioeconomic status and HIV prevalence. Data on antenatal care and labour ward care were obtained from maternal interviews and from reviews of medical records. A total of 665 mother–infant pairs in which the mother was HIV-positive were recruited and 588 (88.4%) were followed up at 3 or 4 weeks postpartum to determine the HIV status and vital status of the infant.

Findings Rural participants were significantly poorer and their health care was significantly worse. Women of higher socioeconomic status and those who received better counselling were more likely to be treated with nevirapine. Rates of early HIV transmission ranged from 8.6% to 13.7%. Maternal viral load was the only statistically significant risk factor for transmission. After adjusting for maternal viral load and prevalence of low birth weight, the odds of transmission were 1.8 times higher at the rural site. Controlling for having had ⩾ 4 antenatal visits and any delivery complication reduced the odds of transmission to 1.5 higher at the rural site.

Conclusion Rates of early transmission of HIV in an operational setting using single-dose nevirapine administered both to mother and child are similar to those obtained in clinical trials. Scaling up access to antiretroviral regimens for women will further reduce transmission to infants.

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Une traduction en français de ce résumé figure à la fin de l'article. Al final del artículo se facilita una traducción al español. الترجمة العربية لهذه الخلاصة في نهاية النص الكامل لهذه المقالة.

Introduction

It has been estimated that out of 1.1 million live births occurring in South Africa in 2002, 69 000 infants (5.9%) were infected with HIV at the time of birth and 20 000 (1.8%) were infected through breastfeeding.[1] In response to these statistics, a programme to prevent mother-to-child transmission was initiated and two pilot sites were established in each of the country's nine provinces. Subsequently, the programme has been expanded to varying degrees in different provinces. By 2004 it was estimated that approximately 45% of women attending antenatal clinics nationally were being tested for HIV.[2]

To minimize mother-to-child transmission of HIV, several critical steps are required. The woman must present at an antenatal care unit; there must be continuity of care to ensure that pre-test counselling and HIV testing are offered and accepted; women must return for their test results; antiretroviral prophylaxis must be administered correctly; women must be screened and offered treatment for other possible risk factors for transmission; safe obstetric practices must be used; appropriate counselling about infant feeding must be offered; and there must be postnatal follow-up. Programme evaluations from several countries in Africa have found deficiencies in various components of preventing mother-to-child transmission (PMTCT) programmes including the uptake of antenatal HIV testing,[3] receipt of test results,[4] uptake of antiretroviral prophylaxis[5–7] and postnatal follow-up of mothers and infants.[8] These deficiencies occur mainly because PMTCT programmes are being introduced into already overburdened health systems.

While there is a substantial body of literature from clinical trials on the efficacy of short-course antiretroviral prophylaxis in reducing transmission from mother to child, data from Africa about the operational effectiveness of national programmes are sparse. One report[9] found that a single-dose nevirapine regimen had a low efficacy in a programme in Nairobi, Kenya, but another from South Africa found an early transmission rate of 8.8%.[10]

Our study measured the rate of early vertical transmission of HIV-1 (that is, transmission of HIV before or around the time of birth) in cohorts of mother–child pairs at three different sites in South Africa that were part of the

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national programme to prevent mother-to-child transmission. We also measured potential risk factors for HIV transmission, including obstetric practices and maternal viral load. A companion paper presents data and risk factors for late transmission.[11]

Methods

Study design

This was a prospective cohort study of mothers and infants seen at three of the 18 national prevention programme pilot sites in South Africa between October 2002 and November 2004. Women were recruited at the health facility either before delivery or within a few days after delivery; they were visited again at 3 to 4 weeks post-delivery.

Study sites

Three areas (the main towns of Paarl and Rietvlei and the dormitory township of Umlazi) were selected to reflect different socioeconomic regions, rural and urban locations and antenatal prevalence rates of HIV. Paarl, in the Western Cape province, is a relatively well-resourced periurban and rural area with a well-functioning health system and a 2004 antenatal HIV prevalence of 9%.[12] Rietvlei, a rural area in the Eastern Cape province, is in one of the poorest parts of South Africa and its antenatal HIV prevalence in 2004 was 28%.[12] Umlazi, near the port of Durban in KwaZulu–Natal, is a periurban area with formal and informal housing. The socioeconomic status of residents is similar to that in Paarl but the health systems are weaker and the antenatal HIV prevalence in 2004 was 47%.[12]

Data collection

All data were collected by trained field researchers. Mothers were interviewed using semistructured interviews at the time of recruitment and during the follow-up visit at 3 to 4 weeks. Topics covered included the extent of antenatal care received, plans for disclosure of HIV status and basic knowledge of HIV/AIDS and of mother-to-child transmission. Obstetric records were reviewed using a record review capture sheet to obtain data on antenatal and intrapartum risk factors for transmission. All interviews were conducted in the preferred language of the participant (Afrikaans, English, Xhosa or Zulu).

Nevirapine was considered to have been taken by the mother according to protocol if it was taken between 2 and 24 hours before delivery; nevirapine was considered to have been administered to infants according to protocol if it was given within 72 hours after birth.

A measure of socioeconomic status was devised using principal component factor analysis that included six household assets (presence of refrigerator, radio, television, stove, telephone or mobile phone, car) and a question regarding food security. This produced a weighted average, so items with a greater variability (e.g. television) contribute more to the score than items with a lesser variability (e.g. radio).

The counselling index measured whether the following three topics were mentioned by the counsellor, nurse or midwife during the woman's pregnancy (as recalled by the woman): the risk of mother-to-child transmission and breastfeeding, how women could choose the best method to feed their infant, and whether the advantages and disadvantages of feeding options were discussed and the woman was helped to make a suitable choice. For each topic a score of 1 was allocated if the topic was covered. If a mother recalled that she was simply told to formula-feed or to breastfeed, then the general counselling index for that mother was decreased by 1 point. Thus, scores on the counselling index ranged from –1 to 3.

During the home visit at 3 to 4 weeks post-delivery, trained field staff collected blood spots on Guthrie cards from all infants and mothers by means of a heel or finger prick. Following overnight drying, the filter paper was inserted into a self-sealing envelope with desiccant. Blood specimens were couriered to the laboratory for analysis.

Laboratory methods

HIV infection in infants was determined from dried blood spots using an HIV-1 RNA quantitation assay (nucleic acid sequence-based amplification with electro chemiluminescent detection, NucliSens HIV-1 QT) with a lower detection limit of 80 copies of HIV RNA per ml of blood (equivalent to 1600 copies HIV RNA per 50 µL dried blood spot)[13] and a qualitative HIV-1 DNA polymerase chain reaction assay (Amplicor HIV-1 Monitor, version 1.5). Infants were defined as infected with HIV-1 if they had a detectable viral load > 10 000 copies/ml or were positive on DNA testing or both.

Mothers' HIV status was determined from their medical records. Women and their infants were recruited prior to or within a few days after delivery and followed until 3 to 4 weeks post-delivery. However, in cases where a mother was recorded as HIV-positive but had no detectable viral load, a repeat enzyme-linked immunosorbent assay was done to check for false positives (Vironostika HIV Uni-form II) followed by Access HIV-1/2 new assay (Bio-Rad). When HIV transmission was calculated, infants born to false-positive mothers were removed from the analysis.

Data entry and management

Quantitative data were entered into a Microsoft Access database using double data entry at a central site (Medical Research Council, Durban). After validation the database was exported to Stata statistical software, version 8.0, for data management and analysis. Comparisons of variables across sites were carried out using χ^2 tests for categorical variables and one-way analysis of variance for continuous variables (with the exception of income, which was compared using a Kruskal–Wallis test). No adjustments were made for multiple testing because the comparison between sites was viewed as descriptive rather than inferential. All factors in Tables 1 and 2 were examined as potential risk factors using logistic regression. To explain differences between the sites, variables were retained in the models if they were either at least of marginal significance or played a confounding role – that is, inclusion of the variable had a noticeable effect (> 10% change) – on the between-site odds ratios.

Ethics

Ethical approval was obtained from the University of KwaZulu–Natal and permission was obtained from participating institutions. Signed informed consent was obtained at the time of enrolment into the study. All staff signed a confidentiality agreement. Compensation offered to participants for their time was site-specific and took the form of cash (Umlazi), food vouchers (Paarl) or food parcels (Rietvlei).

Findings

A total of 665 HIV-positive mother and their infants were enrolled into the study; 588 (88.4%) were followed up at

Table 1. **Baseline characteristics of HIV-positive mothers, their households and infants at three sites in South Africa, October 2002–November 2004**

Baseline characteristics	Study site			*P*-value
	Paarl (*n* = 140)	Rietvlei (*n* = 168)	Umlazi (*n* = 277)	
Maternal characteristics				
Mean maternal age[a] (years)	25.8 (5.2)	24.1 (5.3)	26.1 (5.2)	0.0002
Formal education < 8 years[b]	30 (21.4)	37 (22.8)	46 (17.2)	0.31
Mean maternal log viral load at 3 weeks postpartum[c]	3.98 (0.70)	3.77 (0.78)	3.59 (0.68)	< 0.0001
Household characteristics				
Income (rand/month)[d]	800 (600–1300)	640 (320–860)	700 (400–1200)	Kruskal–Wallis 0.000
Mean socioeconomic score[e]	0.10 (1.53)	−1.37 (1.29)	0.60 (1.42)	< 0.001
Piped water	138 (98.6)	64 (39.0)	276 (99.6)	< 0.0001
Flush toilet	111 (79.3)	2 (1.2)	155 (56.0)	< 0.0001
Electricity or gas used as cooking fuel	81 (57.9)	20 (12.2)	183 (66.1)	< 0.0001
Infants' characteristics				
Mean gestational age at birth[f]	39.4 (1.4)	38.8 (1.8)	38.1 (2.4)	< 0.0001
Mean birth weight[g]	3019 (545)	3018 (497)	3037 (546)	0.91
Low birth weight[h] (< 2500 g)	22 (16.1)	22 (13.6)	38 (13.8)	0.79

[a] Values are age in years (standard deviation).
[b] Values are number (percentage).
[c] Values are mean log viral load (standard deviation).
[d] Values are median income (interquartile range).
[e] Values are mean score (standard deviation). Higher scores of socioeconomic status denote people who have more assets and food security.
[f] Values are number of weeks (standard deviation).
[g] Values are weight in grams (standard deviation).
[h] Values are number with low birth weight (percentage).

3 to 4 weeks postpartum and a specimen of dried blood was obtained.

Women from the rural Rietvlei site generally had lower scores on measures of socioeconomic status (Table 1), attended antenatal clinics later and less frequently and were less likely to have had syphilis tests than women from the two periurban sites (Table 2). The same trends between sites are also apparent in the PMTCT component of maternal care – that is, mothers and infants at Paarl were most likely to receive nevirapine and those from Rietvlei least likely. The composite score of women's reports of the quality of counselling was highest at Umlazi and lowest at Rietvlei.

Logistic regression analysis showed that the higher the socioeconomic status of the mother (regardless of site), the higher the chance of her receiving nevirapine (odds ratio, OR = 1.17 for each 1 point increase in socioeconomic status score, $P = 0.03$). The same analysis also showed that the better the counselling, the greater the chance of the mother receiving nevirapine (OR = 1.55 for a 1 point increase in the counselling index, $P = 0.008$).

A higher proportion of pregnant women in Umlazi had had ruptured membranes for > 4 hours than at the other two sites. The rate of emergency caesarean section was significantly higher in Umlazi than at the other sites and was 10 times higher than in Paarl ($P < 0.0001$). Women at Umlazi also had a significantly higher frequency of delivery complications when compared with the other two sites.

The 3-week HIV transmission rates ranged from 8.6% to 13.7% between sites (Table 3); these differences were not statistically significant.

The only statistically significant risk factor for early transmission of HIV was maternal viral load. A 1-log increase in viral load increased the odds of transmission more than 2-fold. Infants with low birth weight and whose mothers had fewer visits to the antenatal clinic were at a higher risk of becoming infected with HIV, but these factors did not reach statistical significance. There was no association between HIV transmission and a compound measure of socioeconomic status, timing of rupture of membranes before delivery and whether the mother had had an elective caesarean section.

Among the 294 mothers who received nevirapine according to protocol, 29 (9.9%) transmitted HIV to their infants compared with 24 (13.4%) of the 179 mothers who were given nevirapine outside of the time band described in the protocol (that is, it was administered too late or too early). The 113 mothers infected with HIV who were not given nevirapine had a transmission rate of 14.2%. None of these differences achieved statistical significance.

There was no evidence of an association between when the infant received nevirapine and transmission of HIV, but this is probably due to the relatively small number of infants who either did not receive nevirapine or who received it at an incorrect time.

The rate of early transmission was slightly higher among infants who were breastfed than it was among those who were not breastfed (adjusted OR = 1.26), but this difference did not approach statistical significance ($P = 0.49$). It could, however, mean that we have overestimated the rate of early transmission by including some very early transmission that is caused by breastfeeding.

Table 2. **Utilization and quality of maternity care at three sites in South Africa, October 2002–November 2004**

Characteristic of maternity care	Study site			*P*-value
	Paarl (*n* = 140)	Rietvlei (*n* = 168)	Umlazi (*n* = 277)	
Mean no. antenatal visits[a]	5.6 (2.5)	3.3 (1.2)	7.1 (3.2)	< 0.0001
⩾ 4 antenatal visits[b]	106 (75.7)	48 (28.5)	235 (84.8)	< 0.000
Mean gestational age (weeks) at first antenatal visit[c]	23.7 (7.1)	25.7 (4.5)	23.8 (5.6)	< 0.0015
Syphilis test performed[b]	138 (98.6)	48 (28.6)	229 (82.7)	< 0.001
Counselling index[d]	0.97 (0.86)	0.23 (0.56)	1.04 (0.74)	< 0.0001
False-positive rapid HIV test[b]	2/143 (1.4)	7/181 (3.9)	3/279 (1.1)	0.094
Emergency caesarean section[b]	4 (2.9)	21 (12.5)	87 (31.4)	< 0.001
Elective caesarean section[b]	9 (6.6)	14 (8.4)	40 (14.6)	0.02
Rupture of membranes > 4 hours[b]	19 (13.6)	3 (1.8)	80 (28.9)	< 0.001
Delivery complications[b,e]	29 (20.7)	25 (14.9)	183 (66.1)	< 0.001
Mother given nevirapine per protocol[b,f]	95 (67.9)	45 (26.8)	154 (55.6)	< 0.001
Mother given nevirapine late[b]	37 (26.4)	67 (39.9)	75 (27.1)	< 0.001
Mother not given nevirapine[b]	8 (5.7)	56 (33.3)	48 (17.3)	< 0.001
Infant given nevirapine per protocol[b,f]	123 (87.9)	121 (72.0)	210 (75.8)	< 0.001
Infant given nevirapine late[b]	10 (7.1)	18 (10.7)	47 (17.0)	< 0.001
Infant not given nevirapine[b]	7 (5)	29 (17.3)	20 (7.2)	< 0.000
Nevirapine given to mother and infant[b]	126 (90.0)	94 (56.0)	214 (77.3)	< 0.001
Nevirapine given only to infant[b]	7 (5)	45 (26.8)	43 (15.5)	< 0.001
Nevirapine given only to mother[b]	6 (4.3)	18 (10.7)	15 (5.4)	< 0.001
Nevirapine given to neither[b]	1 (0.7)	11 (6.5)	5 (1.8)	< 0.001
Mean number of days from birth to HIV test[g]	24.4 (11.1)	29.5 (10.1)	26.3 (9.7)	< 0.0001

[a] Values are mean number (standard deviation).
[b] Values are numerator (percentage).
[c] Values are mean age in weeks (standard deviation).
[d] Values are mean score (standard deviation). Details of the counselling index are given in the Methods section.
[e] Delivery complications are defined as intrapartum haemorrhage, gestational proteinuric hypertension, eclampsia, cephalopelvic disproportion, poor labour, chorioamnionitis, fever, meconium liquor and fetal distress.
[f] Details of the protocol are given in the Methods section.
[g] Values are mean number of days (standard deviation).

Table 4 shows that when HIV transmission rates by site are adjusted for maternal viral load and low birth weight, the odds of transmission are 1.8 times higher in Rietvlei than in Paarl and 1.6 times higher in Umlazi than in Paarl. The same table also shows which variables partially explain the differences between sites. By controlling for having had ⩾ 4 antenatal visits (which decreases the risk of transmission) and any delivery complication (which increases the risk of transmission), the odds of transmission in Rietvlei become only 1.5 times higher than in Paarl and 1.3 times higher in Umlazi than in Paarl.

The false-positive rate of 2% was due to 13 mothers being recorded as being HIV-positive by the PMTCT programme and being found negative on retesting.

Discussion

The rates of early HIV transmission found across the three sites in a programmatic setting delivering short-course nevirapine were comparable to published results from clinical trials using similar regimens in other parts of Africa (Table 5). The results are better than those from an evaluation in Kenya[9] and similar to those reported by a study near Cape Town, South Africa,[10] and Yaounde, Cameroon.[14]

For the evaluation in Kenya, which looked at the effectiveness of nevirapine in a real-life setting,[9] the authors questioned the effectiveness of ultra-short-term nevirapine administration. They reported that at 14 weeks post-delivery the rate of mother-to-child transmission was 18.1%; this was similar to historical data in the same setting (21.7%) collected before antiretroviral prophylaxis was implemented. However, the Kenyan study had a sample size of only 127 women, used historical controls, had incomplete uptake of nevirapine by mothers (85%) and, by testing at 14 weeks, will have included infants who were infected through breastfeeding.

Table 3. **Number and proportion of infants infected with HIV within 3 to 4 weeks of delivery at three sites in South Africa, October 2002–November 2004**

Site	No. of deliveries to HIV-positive mothers	No. (%) of infants infected with HIV at 3–4 weeks	95% confidence interval
Paarl (*n* = 140)	140	12 (8.6)	4.5–14.5
Rietvlei (*n* = 168)	168	23 (13.7)	8.9–19.8
Umlazi (*n* = 277)	277	33 (11.9)	8.3–16.3

In a cross-sectional study conducted among a settlement of people with low socioeconomic status near Cape Town, South Africa, an early HIV transmission rate of 8.8% was reported from a prevention programme.[10] However, this programme used a predominantly zidovudine-based protocol and this was changed during the study. Nevertheless, the transmission rate is remarkably similar to the 8.6% reported in this paper for the Paarl site, which is also situated near Cape Town.

Authors reporting on the impact of a public health PMTCT programme in Yaounde, Cameroon,[14] found a transmission level of 10.9% at 6 to 8 weeks post-delivery among 119 children born to HIV-positive mothers. It would, therefore, appear that prevention programmes could successfully lower the rate of early transmission of HIV.

It should be noted that the sites in this study were chosen to represent a variety of settings in South Africa. Therefore, it was not surprising that Paarl tended to have the best indicators of health service provision and Rietvlei the worst, with Umlazi falling in between. Some of the differences were quite stark. For example, in Paarl slightly more than two-thirds of women were given nevirapine according to protocol, but less than one-third of the Rietvlei women received nevirapine according to protocol.

The low coverage of nevirapine in Rietvlei occurred primarily because only one clinic in the area was providing PMTCT care, including HIV testing and nevirapine. Thus, most pregnant women were tested only in the labour ward. National data showed a nevirapine coverage rate among HIV-positive women of 43%,[12] suggesting that this component of the programme requires strengthening.

The finding that higher socioeconomic status and a better quality of counselling were associated with an increased chance of the mother taking nevirapine shows the importance of good counselling and the need to pay particular attention to poorer women.

The difference in transmission rates between mothers who received nevirapine and those who did not was small and not statistically significant. However, this is probably because administration of nevirapine to the infant was more consistent and similar across sites and because the infant's dose is particularly critical in avoiding transmission.[15]

Table 4. **Odds ratios (95% confidence intervals) for logistic regression models of risk factors for HIV transmission at 3 weeks at three sites in South Africa, October 2002–November 2004**

Risk factor	Model 1[a] (crude)	Model 2	Model 3	Model 4
Rietvlei used as reference site	1.69 (0.81–3.54) $P=0.16$	1.82 (0.85–3.88) $P=0.12$	1.88 (0.88–4.04) $P=0.105$	1.54 (0.67–3.52) $P=0.31$
Umlazi used as reference site	1.44 (0.72–2.89) $P=0.30$	1.59 (0.77–3.29) $P=0.21$	1.59 (0.76–3.30) $P=0.21$	1.34 (0.61–2.96) $P=0.47$
Log maternal viral load	–	2.13 (1.51–2.99) $P<0.001$	2.09 (1.48–2.94) $P<0.001$	2.08 (1.47–2.94) $P<0.001$
Low birth weight	–	–	1.76 (0.91–3.41) $P=0.095$	1.68 (0.86–3.27) $P=0.13$
⩾ 4 antenatal visits	–	–	–	0.67 (0.35–1.27) $P=0.22$
Any delivery complications	–	–	–	1.41 (0.74–2.67) $P=0.29$

[a] Values are odds ratios (95% confidence intervals).

There was no association between risk of transmission and timing of the maternal or infant dose of nevirapine but, again, this is probably because most infants received the drug and because the timing of administration of maternal and infant nevirapine appears not to be too important as long as it is administered in "reasonable proximity to delivery".[16]

A study has shown that longer regimens of combination antiretrovirals have greater efficacy and can reduce the early transmission rate to as low as 1.1%;[17] such regimens are now recommended by WHO.[18] Our findings suggest that a substantial proportion of women are attending health facilities regularly and may be suitable candidates for longer regimens that could result in better uptake and adherence.

Another striking difference between sites was the finding that caesarean section rates in Umlazi were 10 times higher than in Paarl. This cannot be explained by the type of hospitals found at each site; at all sites the hospital was a district hospital where all deliveries occurred and none were specialist referral hospitals that treated specifically high-risk patients. This finding of a high rate of caesarean section and emergency caesarean section was noted in the SAINT and PETRA trials,[19] and was attributed to "cephalo-pelvic disproportion that is a common obstetric complication in the black population in the province of KwaZulu–Natal", the province in which Umlazi is situated. This is of clinical significance because the SAINT study, but not PETRA, found that emergency caesarean section was associated with a higher risk of HIV transmission to the infant.

Our study showed no association between prolonged rupture of membranes and increased risk of HIV transmission. However, patients with prolonged rupture of membranes are also more likely to undergo caesarean section, and the benefits of this procedure may have balanced out the impact of prolonged rupture. We cannot determine whether this occurred in our study.

The most important risk factor for transmission in this study was the mother having a high viral load. This is not surprising since maternal levels of HIV-1 RNA have been shown in multivariate analyses to be the most important single predictor of intrapartum risk or very early HIV transmission among women who have not received antiretroviral prophylaxis and among women receiving antiretrovirals.[20] Mofenson et al. found no cases of HIV transmission

Table 5. **Comparison of rates of early HIV transmission to infants born to HIV-positive mothers from studies of mother-to-child transmission**

Study	% infants HIV-positive at age 3–4 weeks	% infants HIV-positive at age 5–8 weeks
Current study (Good Start)	11.8	–
PETRA[24]		
Placebo	–	15.3
Regimen A: zidovudine and lamivudine 36 weeks' gestation through 7 days postpartum	–	5.7
Regimen B: zidovudine and lamivudine intrapartum through 7 days postpartum	–	8.9
Regimen C: zidovudine and lamivudine intrapartum only	–	14.2
HIVNET 012[25]		
Zidovudine intrapartum	–	20.0
Nevirapine intrapartum	–	11.8
RETRO CI[26]		
Placebo	21.7	–
Zidovudine from 36 weeks' gestation and intrapartum	12.2	–
Taha T et al.[27]		
Mother and infant treated with nevirapine	–	14.1
Mother treated with nevirapine; infant treated with nevirapine and zidovudine	–	16.3
SAINT[19]		
Nevirapine intrapartum plus for 24–48 hour postpartum	–	12.3
Zidovudine and lamivudine intrapartum plus for 7 days postpartum	–	9.3

among infants born to 84 women who had HIV-1 RNA levels below a detection limit of 500 copies per millilitre.[20] A multisite study involving several African countries has also shown that higher HIV-1 RNA levels in the mother are associated with increased risk of transmission to her child.[18]

Because advanced HIV disease in mothers is associated with poor maternal outcomes, higher viral loads and a higher risk of vertical transmission, the provision of antiretroviral therapy to this subgroup of women will benefit both mothers and children. Integrating a roll-out of antiretrovirals with antenatal care will ensure that mothers requiring antiretrovirals will be referred for treatment.

A potential limitation of our study was that for operational reasons we tested infants for HIV infection at 3 to 4 weeks of age rather than at 6 weeks, as is more commonly done. A concern in regard to testing at 3 to 4 weeks of age is that we may have missed some cases of intrapartum HIV transmission because the testing was done so soon after delivery. However, a meta-analysis of published data from 271 infected children indicated that polymerase chain reaction for HIV DNA was highly sensitive, and that by 14 days after infection, 93% (95% confidence interval: 76–97%) of infected children tested positive by this test.[21] At 28 days after delivery, this had risen to 96% sensitivity and 99% specificity in the ability to identify HIV proviral DNA in peripheral blood mononuclear cells.

The combined use of polymerase chain reaction for HIV DNA and RNA assays for infant diagnosis has not been studied, but from first principles the combining of tests using different technologies should only improve the sensitivity and specificity of the testing algorithm. We are confident, therefore, that we did not miss more than a maximum of 5% of intrapartum infections. Also, an advantage of testing at 3 to 4 weeks in this population is that few cases of transmission by breastfeeding will be included, owing to the short period between birth and testing.

The false-positive rate of 2%, as documented in the prevention programme, is high. This may in part be a result of the test kits used, but the kits comply[22] with WHO's recommendations that rapid HIV tests have a specificity and sensitivity of at least 99%,[23] similar to enzyme-linked immunosorbent assays. In addition to the performance characteristics of these tests, the accuracy of a result depends on numerous factors; these include the skill of the staff performing the tests, the continuous training of staff and the presence of a quality assurance programme that ensures the integrity of standard operating procedures.[23] The highest false-positive rate occurred in Rietvlei, which is where health services had the least resources, although this difference did not reach statistical significance (Table 2).

This study has found that PMTCT programmes using single-dose nevirapine administered to both mother and child are effective in reducing the early transmission of HIV in operational settings. However, when the programme is introduced into already weakened health systems, implementation is not optimal. The data show that maternal viral load is the main risk factor for HIV transmission. This supports calls to scale up antiretroviral regimens targeting pregnant women, both for their own health and to reduce mother-to-child transmission of HIV. ■

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Competing interests: None declared.

Résumé

Efficacité opérationnelle d'une dose unique de névirapine dans la prévention de la transmission de la mère à l'enfant du VIH

Objectif Déterminer l'efficacité opérationnelle du programme de prévention de la transmission de la mère à l'enfant du VIH (PTME) mené en Afrique du Sud dans la réduction des taux de transmission précoce de l'infection.

Méthodes On a choisi comme sujets de l'étude des couples mères-enfants ayant bénéficié du programme PTME pour l'Afrique du Sud entre octobre 2002 et novembre 2004. Ces couples ont fait l'objet d'une étude prospective de cohorte. On a sélectionné trois sites dans des provinces différentes afin de prendre en compte les écarts de statut socioéconomique et de prévalence du VIH. Des entretiens avec les mères et une analyse des dossiers médicaux ont permis d'obtenir des données sur les soins anténatals et ceux dispensés en salle de travail. On a recruté au total 665 couples mères-enfants comprenant une mère séropositive, parmi lesquels 588 (88,4 %) ont été suivis 3 à 4 semaines après l'accouchement pour déterminer le statut vital et le statut à l'égard du VIH du nourrisson.

Résultats Les sujets de l'étude vivant en milieu rural étaient nettement plus pauvres et leur état de santé sensiblement plus dégradé par rapport aux sujets de milieux urbains. La probabilité de recevoir un traitement par la névirapine était plus forte chez les femmes de statut socioéconomique élevé et chez celles ayant été bien conseillées. Les taux de transmission précoce du VIH se situaient entre 8,6 et 13,7 %. La charge virale maternelle s'est révélée le seul facteur de risque ayant une influence statistiquement significative. Après ajustement pour la charge virale et la prévalence des faibles poids à la naissance, la probabilité de transmission du virus pour le site rural était 1,8 fois supérieure à celle en milieu urbain. En contrôlant pour les femmes du site rural ayant bénéficié de 4 visites anténatales au moins et dont l'accouchement s'était opéré sans aucune complication, la probabilité de transmission pour ce site est passée à 1,5 fois celle du site urbain.

Conclusion Les taux de transmission précoce du VIH obtenus dans un contexte opérationnel en administrant une dose unique de névirapine à la mère et à l'enfant sont similaires à ceux enregistrés dans des essais cliniques. L'élargissement de l'accès pour les femmes au traitement antirétroviral permettra de réduire davantage la transmission du VIH aux nourrissons.

Resumen

Eficacia operacional de la dosis única de nevirapina para prevenir la transmisión del VIH de la madre al niño

Objetivo Determinar la eficacia operacional del programa sudafricano de prevención de la transmisión de la madre al niño (PTMN) del VIH en lo que respecta a la reducción de las tasas de transmisión temprana de la infección.

Métodos Se analizó la evolución de pares de madre y lactante que participaron en el programa de PTMN de Sudáfrica entre octubre de 2002 y noviembre de 2004. En este estudio prospectivo de cohortes se seleccionaron tres sitios de diferentes provincias para que estuvieran representados los distintos estatus socioeconómicos y prevalencias de la infección por VIH. Los datos sobre la atención prenatal y en las salas de parto proceden de entrevistas maternas e historias clínicas. Se reclutó a un total de 665 pares de madre y lactante en que la madre era VIH-positiva, lográndose someter a seguimiento a 588 (88,4%) de ellas a las 3 o 4 semanas tras el parto para determinar su serología VIH y el estado del lactante.

Resultados Las participantes rurales eran significativamente más pobres y la atención sanitaria que recibieron fue significativamente peor. Las mujeres de estatus socioeconómico más alto y las que recibieron mejor asesoramiento presentaron una mayor probabilidad de ser tratadas con nevirapina. Las tasas de transmisión temprana del VIH se situaron entre el 8,6% y el 13,7%. La carga viral materna fue el único factor de riesgo de transmisión estadísticamente significativo. Después de ajustar los datos en función de la carga viral materna y de la prevalencia de peso bajo al nacer, la probabilidad de transmisión resultó ser 1,8 veces mayor en el sitio rural. Controlando el número de visitas prenatales (⩾ 4) y las posibles complicaciones del parto, el factor de aumento de la probabilidad de transmisión en el sitio rural se reducía a 1,5.

Conclusión Las tasas de transmisión temprana de la infección por VIH en un entorno operacional de administración de una sola dosis de nevirapina a ambos, madre y niño, son similares a las observadas en ensayos clínicos. La expansión del acceso a los regímenes antirretrovirales para las mujeres reducirá aún más la transmisión a los lactantes.

ملخص

الفعَّالية الميدانية لجرعة وحيدة من النيفيرابين في الوقاية من سراية فيروس الإيدز من الأمهات لأطفالهن

الغرض: التعرُّف على فعالية البرنامج الذي يُنَفَّذ في جنوب أفريقيا للوقاية من سراية فيروس الإيدز من الأمهات لأطفالهن من حيث خفض معدلات السراية الباكرة للعدوى.

الطريقة: شارك في الدراسة مجموعات ثنائية يتألَّف كلٌّ منها من أم وطفلها، في الفترة بين شهر تشرين الأول/أكتوبر 2002 وشهر تشرين الثاني 2004. وكانت دراسة استقبالية للأتراب، اختير فيها ثلاثة مواقع من ولايات مختلفة لتمثيل الأوضاع المختلفة اقتصادياً واجتماعياً ومعدلات انتشار العدوى بفيروس الإيدز. وقد جُمِعَتْ المعطيات حول الرعاية السابقة للولادة والرعاية في قسم الولادة من مقابلات للأمهات ومن مراجعات للسجلات الطبية. وقد حُشِد ما مجموعه 665 من المجموعات الثنائية التي يتشكَّل كلٌّ منها من أم وطفلها، وكانت الأم فيها إيجابية لفيروس الإيدز، وتمَّت متابعة 588 منهم (88.4%) لفترة تتراوح بين 3 و4 أسابيع بعد الولادة لمعرفة أوضاعهم بالنسبة لفيروس الإيدز وفيما إذا بقي الأطفال أحياء.

الموجودات: كان المشاركون من الأرياف أفقر من غيرهم، كما كانت الرعاية التي تُقَدَّم لهم أسوأ بكثير ممن سواهم. أما النساء اللاتي ينتمين إلى طبقة اجتماعية واقتصادية أعلى، واللاتي تلقين نصحاً أفضل من غيرهن، فقد كان

حظهن في تلقّي المعالجة بالنيفيرابين أكبر من غيرهن. وقد تراوحت معدلات السراية الباكرة لفيروس الإيدز من الأمهات لأطفالهن من 8.6% إلى 13.7%، وكان الحمل الفيروسي لدى الأمهات هو عامل الخطر الوحيد الذي يعتد به إحصائياً بالنسبة للسراية، وبعد تصحيح كل من الحمل الفيروسي لدى الأمهات ومعدلات الانتشار للأطفال من ذوي الوزن المنخفض عند الولادة، فإن أرجحية السراية كانت أكثر بمقدار 1.8 أضعاف لدى المواقع الريفية مقارنة بغيرها. وبالنظر إلى من حظين بأربع زيارات أو أكثر قبل الولادة، وتعرضن لأي مضاعفات ولادة، فقد انخفضت أرجحية السراية لتصل إلى 1.5 أعلى مما هو عليه في المواقع الريفية.

الاستنتاج: إن معدلات السراية الباكرة للإيدز في المواقع الميدانية باستخدام جرعة وحيدة من النيفيرابين لكل من الأمهات والولدان كانت متشابهة في التجارب السريرية. إن النهوض بمعدلات إتاحة نظم المعالجة بالأدوية المضادة للفيروسات القهقرية للنساء ستنقص معدلات السراية إلى الولدان أكثر فأكثر.

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