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ORIGINAL ARTICLES

A pilot study to assess the immunologic and virologic efficacy of generic nevirapine, zidovudine and lamivudine in the treatment of HIV-1 infected women with pre-exposure to single dose nevirapine or short course zidovudine and their spouses in Chitungwiza, Zimbabwe

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Abstract

Objective: A pilot study to assess effectiveness of generic Nevirapine (NVP)+Zidovudine (AZT)+Lamivudine (3TC) as potent antiretroviral therapy (ART) in women exposed to either SD NVP or short course (SC) AZT through participation in prevention of mother-to-child transmission of HIV-1 (pMTCT) interventions, and their spouses.

Design: A pilot study of antiretroviral treatment of adults with AIDS.

Setting: Primary health care clinics; Seke North and St Mary's in Chitungwiza, Zimbabwe.

Subjects: Women with pre-exposure to SD NVP or SC AZT and their spouses with CD4 count <200 cells/μL.

Interventions: Generic AZT/3TC twice daily plus NVP daily for the first 14 days and then twice a day thereafter, administered to the cohort.

Main Outcome Measures: The baseline median CD4 count for women and men was 128.5 and 119.0 cells/μL respectively. The geomean virus load was similar for the women and men. At weeks 16, 24 and 48, 82.8%, 85.1% and 73.8% had < 400 copies/ml of HIV RNA respectively. Only at 16 weeks, was the proportion of women (75.9%) with undetectable virus significantly lower than that for men (93.9%), p=0.031. Median CD4 count for both men and women increased significantly, p<0.001. There were no significant differences in virologic responses between the women with pre-exposure to SD NVP and SC AZT. The mean adherence for women and men was similar, >98%.

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Conclusion: Women showed a significantly reduced response to ART relative to men only at week 16. However, prior exposure to SD NVP for PMTCT was no more likely to negatively influence responses to ART than use of SC AZT.

Introduction

Treatment of AIDS with generic antiretroviral therapy (ART) in resource-limited settings often follows *prepartum* maternal regimens; single 200 mg dose (SD) nevirapine (NVP) or a short course (SC) of zidovudine (AZT) as 300 mg twice daily administered to PMTCT.[1] However, use of SD NVP for PMTCT of HIV is associated with the selection of viral resistance. In the HIVNET 012 trial in Uganda, where HIV-1 subtypes A and D predominate, 20% of women exposed to SD NVP had evidence of NVP resistance at six weeks *post partum*, as did 46% of infected infants.[1,2] In the SAINT trial, conducted in South Africa where HIV-1 subtype C predominates, 67% of women given SD NVP during labour and a second dose 24 to 48 hours later had evidence of resistance, with 22% of the women retaining NVP resistance at nine to 12 months *post partum.*[4] In the HIVNET 023 study conducted in Zimbabwe, among women exposed to SD NVP, resistance mutations were identified in 50%, eight weeks *post partum.*[5] In contrast, NVP mutations were observed in only 15% of the women with predominantly HIV-1 subtype B in the US-European PACTG 316 study where women were also receiving highly active antiretroviral drug regimens.[6] The significance of single drug exposure and the selection of resistance for the future treatment of women with AZT and NVP-containing ART are not clear.

The main objective of our pilot study is to assess the immunologic and virologic effectiveness of generic NVP+AZT+3TC in women with pre-exposure to SD NVP or SC AZT through participation in pMTCT intervention programmes and their spouses.

Materials and Methods

Two hundred and fifty three women, their spouses and children, in Chitungwiza, Zimbabwe who had participated in SC AZT or SD NVP programmes for pMTCT enrolled into the Duke cotrimoxazole (CTX) prophylaxis study from 2002 to 2003. Ninety eight of the adults with CD4 cell counts <200 and four children with <20% CD4 cells or WHO adult stage III or IV or paediatric stage III disease, or both met the criteria to initiate CTX prophylaxis as per WHO recommendations.[7] When antiretroviral drugs became available through Medicins Sans Frontieres (MSF) Barcelona, Spain, in 2003, the 98 adults and four children on CTX prophylaxis, who met the national criteria for antiretroviral therapy were offered ART. The study was conducted as a pilot study to assess immunologic and virologic responses among women with pre-exposure to SD NVP or SC AZT and their spouses.

Demographics and medical history were collected and clinical staging of HIV disease was assessed by WHO criteria.[8] Physical examination and laboratory investigations, which included complete blood count with differential, liver function tests, urea and electrolytes were obtained prior to ART, and then at two, four, eight, 12, 16, 24, 36 and 48 weeks. T cell subset profile, and virus load were conducted prior to commencement of ART, then at 16, 24 and 48 weeks.

Whole blood was collected in EDTA tubes in vaccutainers (Becton-Dickinson, Mt View, California). T cell subset profiles were determined by flow cytometry using a Coulter Epics XL equipped with System II software (Beckman Coulter, Miami, Florida, USA) within four hours of blood collection, in the Department of Haematology, College of Health Sciences, University of Zimbabwe. Plasma for virus load quantitation was separated and stored at –80° C within four hours of phlebotomy. Virus load was quantified using Amplicor HIV-1 Monitor assay version 1.5 (Roche Diagnostics Systems, New Jersey, USA) and $\log_{10}$-transformed for subsequent analysis,[9] in the Department of Immunology, College of Health Sciences, University of Zimbabwe. The lower detection limit of this assay is 400 copiesp/ml (<$\log_{10}$ 2.6) copies/ml). Samples collected at 24 and 48 weeks with < 400 copies per ml in the standard assay were re-tested using an ultrasensitive assay with a lower limit of detection of 50 copies/ml. Haematological and biochemical tests were conducted using automated analyzers as per standard methods.

Generic ART comprising duovir (300 mg AZT/150mg lamivudine (3TC), twice a day) plus 200 mg NVP daily for the first two weeks, and then twice a day thereafter (Cipla, Mumbai, India) was provided as first line treatment until June 2004. At that time ART was changed to Avocombivir (AZT plus 3TC, single tablet; Ranbaxy, India) plus NVP (Cipla, Mumbai, India), when Cipla duovir was temporarily de-listed from the pre-approved WHO registry.

Adherence was monitored by the nurses and community lay counsellors by pill count, initially weekly for the first month on ART then monthly thereafter. Percent adherence was calculated at 16, 24 and 48 weeks by dividing the number of tablets taken, by the total number of tablets prescribed. The Batanai community support group (women and men living with HIV or affected by HIV) provided individual and group counselling, to the cohort, as well as psychosocial support prior to commencement of ART and throughout the study.

Statistical Analysis.

In this study, analyses were done to compare data of (i) men versus women and (ii) women with pre-exposure to SD NVP versus those with pre-exposure to SC AZT. The data was analysed to determine whether there were any significant differences in baseline characteristics of men and women using STATA version 7 (College Station, Texas, USA) and SPSS version 12 for windows (SPSS INC., Chicago, Illinois, USA) and the significance level for this analysis was set at 5%.

For continuous variables such as age the assumption of normality was checked. If the variable was normally distributed the independent t-test was used for gender-based comparisons. If the assumptions were not met then the non-parametric test (Mann-Whitney U test) was used.

Analysis of variance was also used to compare continuous variables over the four time points. The Bonferroni correction was used to account for multiple comparisons and determine significance over time. If the data was not normally distributed, then the non-parametric equivalent of ANOVA, the Kruskal Wallis was done. The 95% confidence interval (CI) were also used to estimate the precision of the estimated parameters. For the discrete variables the Chi-squared test was used to test the association for each variable between the two groups, i.e. (i) men versus women and (ii) women with SD NVP pre-exposure versus those with SC AZT pre-exposure).

Role of Funding Source.

The study was supported by a grant from the Doris Duke Charitable Foundation, which did not have a role in data collection, analysis, data interpretation, or writing of the manuscript. No pharmaceutical sponsors were involved.

Results

Study Cohort.

Ninety eight patients comprising 62 women and 36 men commenced generic ART between July 2003 and December 2004, in Chitungwiza, Zimbabwe (Figure I). Eleven patients did not reach week 16 for the following reasons; one woman died of presumed clinical pneumocystis pneumonia four weeks after commencing ART, four patients refused further treatment; four patients were lost to follow up when they moved out of Chitungwiza and could not be traced, and two patients were discontinued (1 week after initiating ART) by the study physicians as they had been commenced on ART in error (CD4 count >200cells/mL and WHO stage I disease).

Of the 87 subjects, all had CDC-defined AIDS based on a CD4 count <200 cells/mL, 40 (46.0%) were asymptomatic (WHO stage I disease); 15 (17.2%) had WHO stage II disease while 32 (36.8%) had AIDS-defining conditions (WHO stages III and IV). Thirty four and 20 women had pre-exposure to SC AZT or SD NVP respectively through participation in pMTCT interventions between 1999 and 2003. The estimated median time from SC AZT and SD NVP pMTCT intervention to commencement of ART was 36 months (IQR: 24 to 48) and 17 months (IQR: 12 to 30) respectively, p=0.001. The baseline demographics of the 87 subjects are shown in Table I.The median age of the 54 women was significantly lower than that of the 33 men (p=0.003). There were no other statistically significant differences in baseline characteristics between the 54 women and the 33 men.

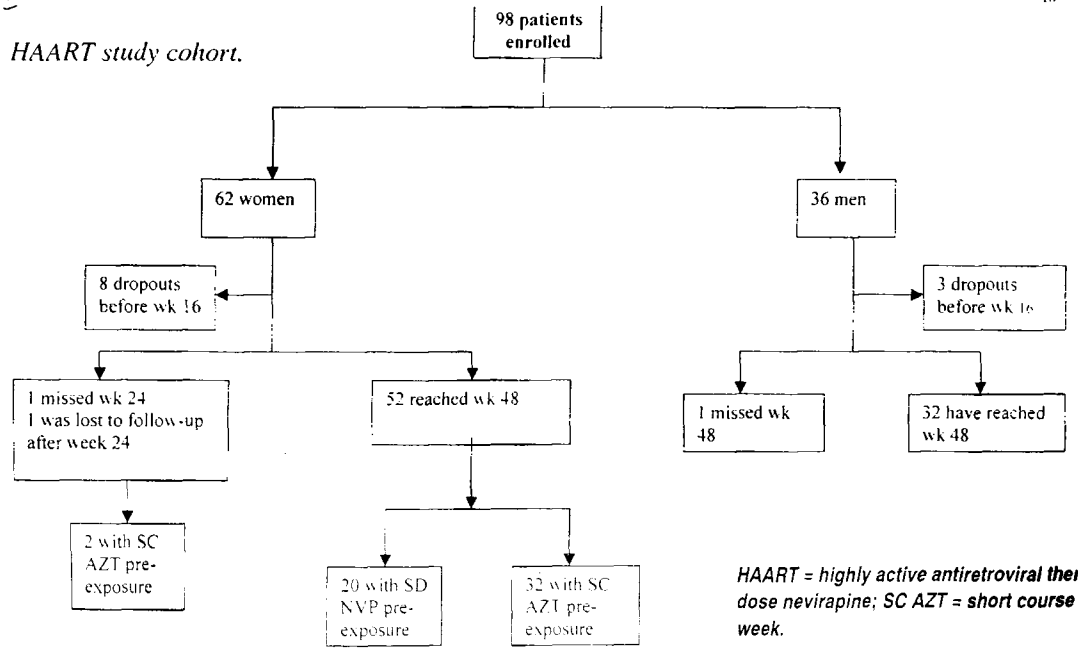
Immunologic and Clinical Responses of the 87 Patients on ART.

At baseline, the median CD4 counts for women and men were not significantly different; 128.5 (Interquartile Range [IQR]: 72.0 to 177.0) and 119 (IQR: 70.0 to 160.0) cells/?L respectively, p=0.401 (Table I). There was a significant increase in median CD4 counts from baseline to week 48 for both women and men p<0.001 (Table II) inversely correlated with a decrease in geometric mean virus load. The mean weight for the cohort increased statistically significantly (p=0.018). Further analysis with a Bonferonni correction showed that the increase was statistically amongst men (p=0.001), but not women (p=0.087). Among the men, a statistically significant increase occurred between 0 and 16 weeks (p=0.037) , between 16 and 24 weeks (p=0.009) and between 24 and 48 weeks (0.002). The mean adherence throughout the study period was greater than 98% and did not differ significantly between men and women.

Virologic Responses at Weeks 16, 24 and 48.

The geometric mean (GMT) virus load at baseline for women and men was similar: 5.0 $\log_{10}$ copies/ml, p=0.63

Figure I. HAART study cohort.



HAART = highly active antiretroviral therapy; SD NVP = Single dose nevirapine; SC AZT = short course zidovudine; wk = week.

Table I: Baseline characteristics of the 86 adults who have reached week 48 following commencing of HAART.

Characteristic	All (n =86)	Females (n = 53)	Males (n =33)	*p (males vs females)
Mean age (years) ± SD (CI)	33.3 ± 5.4 (32.1-34.4)	31.9 ± 4.6 (30.6-33.2)	35.5 ± 5.9 (33.4-37.5)	0.003
Mean weight (kg) ± SD (CI)	59.7 ± 8.7 (CI: 57.8-61.5)	58.3 ± 8.8 (CI: 55.9-60.7)	61.9 ± 8.1 (CI: 59.0-64.8)	0.065
WHO stage I	39 (45.3%)	22 (41.5%)	17 (51.5%)	
WHO stage II	15 (17.4%	9 (17.0%)	6 (18.2%)	
WHO stage III and IV	32 (37.2%)	22 (41.5%)	10 (30.3%)	0.501
Mean Hb (g/dL) ± SD (CI)	N/A	11.4 ± 1.4 (11.1-11.8)	13.1 ± 1.6 (12.6-13.7)	N/A
Median ALT (IU/L) (IQR)	28.0 (19.0-39.0)	27.5 (19.0-34.0)	30.0 (18.0-40.0)	0.373
Median CD4 (cells/?L) (IQR)	123.0 (70.0-175.0)	128.5 (72.0-177.0)	119.0 (70.0-160.0)	0. 401
Median CD8 (cells/?L) (IQR)	582.0 (375.0-758.0)	588.5 (418.0-756.0)	512.0 (318.0-827.0)	0.576
CD4:CD8 ratio (IQR)	0.2 (0.1-0.3)	0.2 (0.2-0.3)	0.2 (0.1-0.3)	0.850
Median lymphocytes cells/?L (IQR)	996.0 (710.0-1354.0)	1 029.5 (728.0-1277.0)	912.0 (710.0-1370.0)	0.603
Median neutrophils (x 10^9 cells/L) (IQR)	1.36 (1.02-2.04)	1.38 (0.97-2.13)	1.36 (1.10-1.69)	0.913
Geomean Log_{10} virus load (copies/ml) (IQR)	5.0 (4.5-5.4)	5.0 (4.3-5.3)	5.0 (4.7-5.4)	0.63

ALT= alanine aminotransferase; Hb = Haemoglobin; HAART = highly active antiretroviral therapy; IQR = interquartile range; n = number; *p = p value, calculated using the student T-test and Kruskal-Wallis test for normally — and not normally-distributed variables respectively. p values <0.05 were considered statistically significance; N/A = not applicable, normal reference ranges are gender sensitive.

Table II: Characteristics of HAART patients at baseline, 16, 24 and 48 weeks.

Characteristic	Gender	Time (weeks) Baseline (N = 87)	16 (N = 87)	24 (N =87)	48 (N =84)	*P* value
Median CD4: (cells/mL) (IQR)	Females	128.5 (72.0-177.0)	244.0 (159.0-336.0)	253.0 (180.0-323.0)	287.0 (203.5-395.5)	<0.001[a]
	Males	119.0 (70.0-160.0)	221.0 (151.0-327.0)	226.0 (160.0-310.0)	239.0 (177.0-309.0)	<0.001[a]
	All	123.0 (70.0-175.0)	239.0 (153.0-336.0)	252.5 (171.0-319.0)	265.0 (187.5-345.5)	<0.001[a]
Mean weight: kg ± SD (CI)	Females	61.4 ± 8.4 (59.1-63.7)	58.8 ± 9.7 (56.2-61.5)	60.2 ± 10.3 (57.4-63.1)	63.8 ± 12.2 (60.4-67.2)	0.087[b]
	Males	56.9 ± 8.5 (53.9-59.9)	62.5 ± 7.5 (59.8-65.2)	63.4± 8.1 (60.5-66.3)	64.3 ± 8.4 (61.2-67.4)	0.001[b]
	All	59.7 ± 8.7 (57.8-61.5)	60.2 ± 9.1 (58.2-62.1)	61.4 ± 9.6 (59.4-63.5)	64.3 ± 10.7 (61. 2-67.4)	0.018[c]
Mean % adherence ± SD (CI)	Females	Not applicable	98.3 ± 6.1 (96.6-100)	98.7 ± 4.3 (97.5-99.9)	99.1 ± 2.3 (98.5-99.7)	0.678[c]
	Males	Not applicable	98.9 ± 2.4 (98.1-100)	98.4 ± 2.2 (97.6-99.2	99.0 ± 1.0 (98.6-99.4)	0.385[b]
	All	Not applicable	98.5 ± 4.9 (97.5-99.6)	98.6 ± 3.7 (97.8-99.4)	99.0 ± 1.9 (98.5-99.5)	0.596[b]

HAART = highly active antiretroviral therapy; IQR = interquartile range; n = number; CI = 95% confidence interval, SD = standard deviation.
[a] = p value calculated to detect changes within each gender from baseline to week 48 using Kruskal-Wallis test for not normally distributed variables.
[b]= p value calculated to detect changes within each gender from baseline to week 48 using analysis of variance (ANOVA).
p values <0.05 were considered statistically significance; N/A = not applicable, normal reference ranges are gender sensitive.

(Table I). At 16 weeks, 72 subjects (82.8%), 41 women and 31 men, had less than 400 copies/mL of HIV RNA (Table III). There was a statistically significant difference in the proportion of women (75.9%) and men (93.9%) with less than 400 copies of HIV RNA, p=0.031 (Table III). Seventeen of the 20 women (85.0%) with pre-exposure to SD NVP had undetectable virus at 16 weeks, while the 29 women out of 34 (85.3%) with undetectable virus had pre-exposure to SC AZT, p=0.977 (Table IV). Two men of the 33 (6%) had detectable virus at week 16 which persisted throughout the study period.

At 24 weeks, 74 subjects (85.1%), 44 women (81.5%) and 30 men (90.9%), had less than 400 copies/ml of HIV RNA, p=0.231 (Table III). Using the ultrasensitive assay (US) with a lower detection limit of 50 copies/ml, 60.9% subjects, 33 women (61.1%) women and 20 (60.6%) men had undetectable virus, p =0.963 (Table III). Of the 44 women with less than 400 copies/mL HIV RNA, 28 (82.4%) had pre-exposure to SC AZT while 16 (80.0%) had pre-exposure to SD NVP, p=0.830. By US assay, 33 women comprising 21 (61.8%) with pre-exposure to SC AZT and 12 (60.0%) with pre-exposure to SD NVP, p=0.898 had undetectable virus (Table IV).

At 48 weeks, 62 (73.8%) subjects, 36 women and 26 men had less than 400 copies HIV RNA. The percentage of women (69.2%) with more than 400 copies/ml of HIV RNA was not significantly different from that for men (81.3%) with undetectable virus, p=0.224 (Table III). Similarly, using the US assay with a lower detection limit of 50 copies/ml, the percentage of women (69.2%) with less than 50 copies/ml of HIV RNA was not significantly different from that of men (81.3%) with undetectable virus, p=0.064. There was no statistically significant difference in the frequency of rebound viremia between the 13 women (25.0%) and five men (15.6%) p=0.309 when the US assay with a lower detection limit of 50 copies/ml was performed in later samples. Of the 25 women with less than 50 copies/ml HIV RNA, 16 (16/32)

Table III: Comparison of proportions of women and men with undetectable virus at weeks 16, 24 and 48.

		Gender		
Weeks	**All N (%)**	**Women N (%)**	**Men N (%)**	**P value***
16 (<400 copies/mL)[a]	72 (82.8) N = 87	41(75.9%) N = 54	31 (93.9) N = 33	0.031
24 (<400 copies/mL)[a]	74 (85.1) N = 87	44 (81.5%) N = 54	30 (90.9) N = 33	0.232
24 (<50 copies/mL)[b]	53 (60.9) N = 87	33 (61.1) N = 54	20 (60.6) N = 33	0.963
48 (<400 copies/mL)[a]	62 (73.8%) N = 84	36 (69.2%) N = 52	26 (81.3) N = 32	0.221
48 (<50 copies/mL)[b]	47 (55.6%) N = 84	25(48.1) N = 52	22 (68.8) N = 32	0.064

p value indicates comparison of women versus men. [a] The standard Roche Amplicor HIV-1 monitor test with a lower detection of 400 copies/ml was used. [b] The ultrasensitive Roche Amplicor HIV-1 monitor test with a lower detection of 50 copies/ml was used.

Table IV: Proportion of women with undetectable virus at weeks 16, 24 and 48 stratified by pMTCT ARV pre-exposure.

	PMTCT ARV Pre-exposure		
Weeks	**SC AZT N(%)**	**SD NVP N(%)**	**p value***
16 (<400 copies/mL)[a]	29 (85.3) N = 34	17(85.0) N = 20	0.977
24 (<400 copies/mL)[a]	28 (82.4)	16 (80.0)	0.830
24 (<50 copies/mL)[b]	21 (61.8) N = 34	12 (60.0) N = 20	0.898
48 (<400 copies/mL)[a]	23 (71.9)	13 (65.0)	0.601
48(<50 copies/mL)[b]	16 (50.0) N = 32	9 (45.0) N = 20	0.726

ARV = antiretroviral therapy; pMTCT = prevention of mother-to-child transmission of HIV; SC AZT = short course AZT; SD NVP = single dose nevirapine; AZT.. [a] The standard Roche amplicor HIV-1 monitor test with a lower detection of 400 copies/mL was use. [b] The ultrasensitive Roche amplicor HIV-1 monitor test with a lower detection of 50 copies/ml was used. p value* indicates comparison of women with pre-exposure to SD NVP versus women with pre-exposure to SC AZT.

had pre-exposure to SC AZT (50.0%) and nine (9/20) had pre-exposure to SD NVP (45.0%), p=0.726 (Table IV).

The mean adherence for the cohort was ≥98% throughout the study period. There were no significant differences in mean adherence between men and women (Table II).

Discussion

Generic ART with nucleoside reverse transcriptase inhibitors (NRTI) and a non-nucleoside reverse transcriptase (NNRTI) inhibitor are increasingly being used in resource-limited countries for treatment of AIDS. A few studies have reported on the effectiveness of these drugs.[10,15] The WHO recommends NVP or EFV combined with a thymidine analog (either AZT or d4T) and lamivudine (3TC) as the practicable and affordable first-line therapy for treatment of HIV disease.[8] because of cost and feasibility of twice daily NNRTI-containing ART regimen as well as availability of pharmacokinetic and safety data in adults. The WHO has also recommended the use of SD NVP as an intervention for pMTCT in resource-poor countries, particularly where alternative regimens are not available.[8] However, the use of SD NVP has been reported to induce high level of drug resistance to NVP and other NNRTIs.[2-5] The clinical relevance of NNRTI resistance mutations following administration of SD NVP is not known. However, a recent large double-blind clinical trial conducted in Thailand which examined subsequent maternal responses to NVP-based ART in women who received SC AZT and intrapartum SD NVP exposure for pMTCT reported that after 24 weeks of treatment with NVP-containing ART, 49% of women with pre-exposure to SD NVP had virus load of less than 50 copies/ml compared to 68% with no *intrapartum* SD NVP exposure.[16,17]

In this pilot study, we compared immunologic and virologic responses to a NVP — and AZT-containing ART regimen between women with pre-exposure to either SD NVP or SC AZT. There were no statistically significant differences in immunologic and virologic responses to generic NVP-containing ART between the 20 women with SD NVP and 33 women with SC AZT pre-exposure. Due to limited resources, we do not yet have data on NVP or AZT mutations following exposure to SD NVP or SC AZT in this cohort. However, although several studies have reported development of NVP resistance following administration of SD NVP,[2-6] SC AZT for pMTCT of HIV in Cote d'Ivoire, was not associated with the development of detectable drug resistance.[18]

The Thai study showed that women with pre-exposure to SC AZT and SD NVP had reduced virologic response rates compared to those with SC AZT pre-exposure only.[16,17] The results presented here, as compared to the Thai study may be very different for several reasons. First, HIV-1 infection in Zimbabwe is largely due to subtype C HIV-1[19] Second, there was a key difference between the timing of ART, relative to pMTCT intervention and delivery. In Thailand, women were offered treatment a median of five months *post partum*, whereas the women in our study were offered ART an estimated median of 17 or 36 months after SD NVP or SC AZT respectively. The higher virologic failure rates among women treated within months of NVP for pMTCT in the Thai study are consistent with the higher frequency of resistant mutants following SD NVP exposure and their subsequent "fading" (becoming undetectable in consensus sequence in most women) one year after SD NVP exposure.[3] Third, it is important to note that overall, the results presented here, with respect to virologic suppression among women, using either the assay with a lower detection limit of 400 copies/ml or 50 copies/ml, do reflect the differences in timing of treatment and sensitivity of the virologic assays. Jourdain and colleagues reported less than 400 copies/ml of HIV RNA among 85% and 76% of women who were exposed to AZT and SD NVP

respectively[20] while we found less than 400 copies/ml of HIV RNA in 78% and 70% among those with more remote exposure to SC AZT and SD NVP respectively. Using a more sensitive assay with a lower detection limit of 50 copies/ml, the frequency of virologic suppression at six months in Thailand was 46% among those exposed to NVP, and 74% with AZT alone. In Zimbabwe, these rates were 45% and 50% among women who had received SD NVP and SC AZT respectively. Extrapolation of our results is limited as this is only a pilot study limited by the small size of the cohort. Clearly, larger studies are required to establish if the period between NVP exposure and commencement of NVP-based HAART regimen influences immunologic and virologic responses.

The virologic response to generic ART in our study is comparable to that reported by a few other studies conducted in Africa and India, albeit using different generic regimens. In our study, at 24 weeks, 74 out of 87 patients (85.1%) had a virus load below 400 copies/ml, compared to 48 out of 60 patients (80%) in Cameroon on a generic fixed dose combination of 3TC/d4T/NVP.[10] In a South African study of 20 patients who completed 52 weeks on generic NVP/d4T/3TC, 86% had virus load below 400 copies/ml and 74% had a virus load below 50 copies/ml.[14] A study in India reported that 38 out of 40 patients (95%) on a generic fixed dose combination of EFV/AZT/3TC had virus load below 400 copies/ml at week 24.[15] In our study, at week 48, 62 out of 84 (73.8%) had virus load below 400 copies/ml while 55.6% had a virus load below 50 copies/ml.

The overall mean adherence of 98% throughout the study period, is comparable to that reported from studies conducted in resource-poor countries using either proprietary or generic antiretroviral regimens[10, 21, 22] but somewhat higher than that reported in the resource-rich countries using proprietary antiretroviral regimens.[23-25] The immunologic and virologic responses in our study subjects may be attributable to the high adherence, achieved through the involvement of community lay counsellors who themselves are people living with HIV or AIDS who not only monitored adherence but also provided psychosocial support prior to commencement of ART and throughout the study period. In terms of evidence for lack of virologic efficacy of ART, eight women (five with pre-exposure to SC AZT and three with pre-exposure to SD NVP) and two men had detectable virus at all four laboratory evaluations. The median adherence of these patients, or that of the patients who initially suppressed with re-bound viremia at subsequent visits was not significantly different from that of the rest of the cohort. Good adherence to ART has been associated with enhanced immunologic and virologic responses.[26] Here, we cannot attribute the poor virologic response to poor adherence and it remains to be established whether drug resistance prior to commencement of ART, or differences in adsorption, metabolism or the pharmaco-dynamics of the drugs, may explain virologic failure. It has been suggested that in resource-poor countries, clinical alternatives to sophisticated laboratory monitoring of ART may include serial measures of weight.[27] In our small cohort, there was a statistically significant increase in weight, from baseline to 48 weeks among men, but not among women. Gender-based differences in viral pathogenesis and response to ART are controversial[28] and references therein]. Among very different populations of HIV infected individuals in North America, recent studies conclude that there are no statistically significant biological gender-based differences in response to ART. Rather psychosocial factors such as illicit drug use and incomplete ART adherence may be responsible[28,29] and in Africa, women may be subject to differential psychosocial and economic pressures.[30] More complex gender-based barriers to successful treatment in Zimbabwe, including the socio-economic status of women, their child-care and occupational responsibilities and issues around disclosure and family support need further and more intensive study.

Conclusion

Generic ART administered and monitored by nurses and community lay counsellors is feasible and effective in the treatment of AIDS in resource limited settings in Africa. Involvement of community lay counsellors and support groups in the community contributed to a pronounced benefit in reducing mortality with robust immunologic and virologic responses, even among highly marginalized people with very limited resources. Although limited in size, our pilot study suggests that that use of SD NVP for pMTCT of HIV is no more likely to negatively influence immunologic and virologic responses to a NVP-containing ART regimen than use of SC AZT.

Conflict of Interest Statement.

None declared.

LSZ, corresponding author, had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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