Research Article

A prospective study of highly active antiretroviral therapy in a tertiary-care hospital in south India

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Abstract

Background: Acquired immunodeficiency syndrome (AIDS) caused by human immunodeficiency virus (HIV) is an important health concern worldwide, and AIDS-related morbidity and mortality have seen a sharp decline due to the introduction of highly active antiretroviral therapy (HAART). To address the problems of high cost, poor compliance, lack of awareness, social stigma, and occurrence of adverse effects in India, National AIDS Control Organization (NACO) has organized a simplified drug regimen with regular monitoring, counseling, and follow-up by specially trained personnel with necessary laboratory facilities and infrastructure.

Objectives: The present study was taken up to assess the efficacy of the NACO-recommended HAART regimen in subjects with HIV in the south Indian population.

Materials and Methods: HAART, consisting of two nucleoside reverse transcriptase inhibitors and one non-nucleoside reverse transcriptase inhibitor, was instituted in 158 properly selected subjects. The initial therapy in most of the subjects was zidovudine (AZT) + lamivudine (3TC) + nevirapine (NVP). AZT was substituted by stavudine (d4T) in patients with Hb % < 8 g, whereas NVP was substituted by efavirenz (EFV) in the event of non-availability, adverse effects, or possible interactions. All subjects received cotrimoxazole prophylaxis. Patients were monitored at regular intervals for 24 weeks. Efficacy was assessed by response based on CD4 count; total lymphocyte count; and improvement assessed in terms of general health, weight gain, functional status, and improvement in WHO clinical staging.

Results: There was good clinical improvement with increase in CD4 count in the majority of the subjects. Antiretrovirals were well tolerated, with only mild, tolerable, and controllable adverse events, and death occurred only in 5.71% the subjects.

Conclusion: The NACO-sponsored HAART regimen was found to be effective and well tolerated in the majority of the subjects, with minimum and tolerable adverse effects.

KEY WORDS: Acquired immunodeficiency syndrome (AIDS), human immunodeficiency virus (HIV), highly active antiretroviral therapy (HAART), efficacy

Introduction

Acquired immunodeficiency syndrome (AIDS) caused by human immunodeficiency virus (HIV) is a major global health problem, affecting nearly 33.3 million people worldwide, with an adult incidence of about 30.8 million. The current HIV prevalence in India is 0.31% of the adult population (23.9 lakhs), of which 39% are women and 3.5% are children, and most infections occur through heterosexual route of transmission.[1]

The global approach to the problem of HIV/AIDS is mainly to reduce transmission by improving public awareness through proper health education, to reduce morbidity and mortality by effective therapy, and to minimize the socio-economic impact. The use of highly active antiretroviral therapy (HAART) has led to a dramatic decline in AIDS-related morbidity and mortality, and has helped control viral replication and prevent the possibility of rapid emergence of permanent drug resistance. Although HAART does not cure HIV infection, it decreases viral load and improves the immunological status. However, HAART involves a high cost, lifelong therapy, and occurrence of adverse effects. In this regard, Government of India constituted National AIDS Control Organization (NACO) in 1992 and launched a scheme providing free ART from April 2004.[1]

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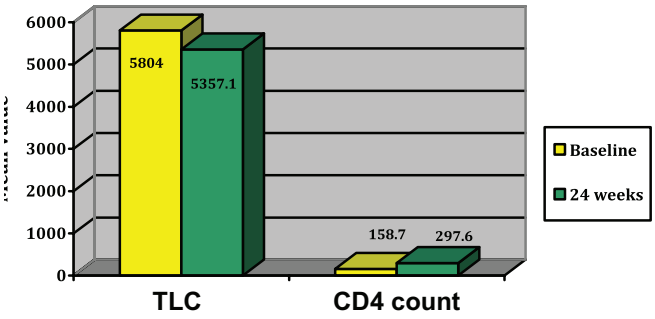

Figure 1: Mean CD4 count and TLC of subjects on AZT + 3TC + EFV

The aim of this study was to assess the efficacy of the NACO-recommended HAART regimen in subjects with HIV in the south Indian population.

Materials and Methods

This prospective study was conducted at the ART Center at Kempegowda Institute of Medical Sciences, Bangalore. The study conformed to the ICH-GCP guidelines and the Declaration of Helsinki, and was approved by the institutional ethics committee and NACO.

Study design

This study was conducted between January 2010 and June 2011 with purposive sampling, involving 158 subjects who received HAART. Subjects of either gender aged between 18 and 65 years with confirmed HIV infection (as screened by a rapid immunoassay test [TRI-DOT] and further confirmed by ELISA using two types of antigens recommended by NACO) were included in the study. WHO clinical staging of stages I and II (CD4 count <350 cells/mm^3) and stage III (irrespective of CD4 count) was performed. Subjects already on HAART, asymptomatic subjects with CD4 count >350 cells/mm^3, pregnant and lactating women, subjects with preexisting severe opportunistic infections (WHO stage IV), and subjects who may not be available for regular follow-up such as migrants and nomadic tribes were excluded.

Written informed consent was obtained from all the study subjects after fully explaining the details of the study, in both English and vernacular, to their satisfaction, after assuring them of complete anonymity, confidentiality, and professional secrecy.

Study procedure

Demographic data, clinical history, relevant clinical data, and results of laboratory investigations were recorded. Study subjects received HAART as per the NACO guidelines, consisting of zidovudine (AZT) (300 mg BID)/stavudine (d4T) (30 mg BID) + lamivudine (3TC) (150 mg BID) + nevirapine (NVP) (200 mg OD)/efavirenz (EFV) (600 mg OD). All these drugs were used as fixed-dose combinations and subjects were advised to take medications after meals to avoid gastric irritation; however, EFV was administered separately whenever used, the preferred initial therapy being based on hemoglobin (Hb) status and liver function tests. AZT was substituted by d4T in subjects with Hb% <8 g, and NVP was substituted by EFV in subjects with clinical hepatitis/raised ALT (>5 times the upper normal limit). Any further change in the regimen or drug substitutions was also recorded. In subjects receiving NVP, dose was increased from 200 mg OD to 200 mg BID after 2 weeks in the absence of any occurrence of rashes. All the study subjects received cotrimoxazole prophylaxis (960 mg OD) from baseline till the CD4 count increased to >350 cells/mm^3. In addition, subjects with mild opportunistic infections such as diarrhea and respiratory tract infections also received cotrimoxazole (960 mg OD) for 5–7 days. All ARVs were supplied free of cost to the subjects by NACO.

The efficacy of HAART was assessed by treatment response based on CD4 count; total lymphocyte count; and clinical improvement assessed in terms of general health, weight gain, functional status, and improvement in WHO clinical staging. Opportunistic infections occurring during the course of therapy and the treatment instituted for the same were also recorded.

For subjects receiving AZT, Hb% was estimated for early detection of anemia, and for those receiving NVP, alanine aminotransferas (ALT) levels were assessed for any evidence of hepatitis at 2, 4, 8, and 12 weeks.

Subjects receiving HAART were monitored and counseled at regular visits, initially after 2 weeks (to consider escalation of nevirapine dose in the absence of any intolerance), followed by monthly visits up to 24 weeks. Follow-up was extended beyond 24 weeks for subjects who were lost to follow-up during the last 12 weeks of the follow-up period. Medications were dispensed to subjects directly with proper instructions and counseling. Outreach field workers were also employed to assist the subjects from remote or rural areas.

Statistical analysis

Data collected were analyzed by using descriptive statistics, namely, mean, standard deviation (SD), standard error of mean (SEM), *t*-test, and confidence intervals (CIs), for quantitative variables using SAS 9.2 and SPSS 15.0 programs.

Results

A total of 158 subjects were recruited for the study [men = 103 (65.18%), women = 55 (34.82%)]. The mean age of the study subjects was 36.13 ± 8.52 years and majority of the study subjects (*n* = 130, 82.27%) were aged between 26 and 45 years.

Antiretroviral drugs were used in combination, consisting of two nucleoside reverse transcriptase inhibitors (NRTIs) and one non-nucleoside reverse transcriptase inhibitor (NNRTI), as per the NACO guidelines (Table 1). The NRTIs included AZT, 3TC, and d4T, whereas NNRTIs included NVP and EFV.

The preferred initial regimen or first-line option recommended by NACO was AZT + 3TC + NVP (*n* = 148, 93.7%).[2] However, at the baseline visit, AZT was required to be substituted by d4T because of anemia (*n* = 6, 3.8%) and NVP

Table 1: Subjects on HAART regimen as per the NACO guidelines [*n* (%)]

	AZT + 3TC + NVP*	d4T† + 3TC + NVP	AZT + 3TC + EFV‡	d4T + 3TC + EFV	NA§
Baseline‖	148 (93.7%)	6 (3.8%)	4 (2.5%)	—	—
2 weeks	136 (86.1%)	12 (7.6%)	8 (5.1%)	—	2 (1.3%)
4 weeks	118 (74.7%)	12 (7.6%)	20 (12.7%)	—	8 (5.1%)
8 weeks	85 (53.8%)	19 (12%)	38 (24.1%)	—	16 (10.1%)
12 weeks	63 (39.9%)	24 (15.2%)	46 (29.1%)	3 (1.9%)	22 (13.9%)
16 weeks	61 (38.6%)	23 (14.6%)	49 (31%)	3 (1.9%)	22 (13.9%)
20 weeks	51 (32.3%)	23 (14.6%)	58 (36.7%)	3 (1.9%)	23 (14.6%)
24 weeks	51 (32.3%)	24 (15.2%)	59 (37.3%)	3 (1.9%)	21 (13.3%)

*NVP escalated from 200 mg OD to 200 mg BID after 2 weeks in subjects without any intolerance.
†AZT substituted by d4T because of anemia.
‡NVP substituted by EFV because of either NACO being out of NVP supply or due to SJS.
§Not available for follow-up at the scheduled visits or lost to follow-up, or deceased.
‖Initial therapy and all subjects received cotrimoxazole prophylaxis till CD4 count increased to >350 cells/mm^3.

was to be substituted by EFV (*n* = 4, 2.5%) because of its non-availability in NACO supply. The dose of NVP was increased from 200 mg OD to 200 mg BID after 2 weeks, except in one subject who developed Stevens–Johnson syndrome (SJS) within a week after treatment initiation. During subsequent follow-up visits, some subjects under AZT-based regimen were shifted to d4T-based regimen because of development of anemia (Table 1). Six subjects under NVP-based regimen who developed SJS (*n* = 5, 3.2%) and hepatitis (*n* = 1, 0.6%) were also shifted to EFV-based regimen. At the end of 24 weeks, only 51 subjects (32.3%) were under AZT + 3TC + NVP regimen, 27 subjects (17%) were under d4T-based regimen, and 62 subjects (39.2%) were under EFV-based regimen. Twenty-one (13.3%) subjects were not available for follow-up, of which nine subjects (5.7%) were known to be deceased.

The majority of the subjects (*n* = 148, 93.67%) were without any comorbid illnesses. Medications used for comorbid conditions included atenolol (*n* = 2, 1.3%), furosemide, atorvastatin + clopidogrel + furosemide, atorvastatin + clopidogrel + metoprolol + ISDN, glibenclamide + metformin, human insulin, L-thyroxine, pantoprazole, and telmisartan + HCTZ + metformin (each *n* = 1, 0.6%).

Table 2 shows the treatment outcome based on improvement in WHO staging and clinical parameters at the end of 24 weeks. With regard to treatment outcome, the number of subjects with stage III according to WHO staging was reduced from 30 (19%) at baseline to 11 (7%), and that of subjects with stage II reduced from 66 (41.8%) at baseline to 8 (5%), whereas that of subjects with stage I at baseline increased from 62 (39.2%) to 119 (75.3%) after 24 weeks, indicating a decrease in the severity of the illness. However, two subjects progressed to stage IV after 24 weeks. Although there was very little improvement (4.67%) in mean body weight at the end of 24 weeks, the mean improvement in body weight appeared to be more significant in AZT + 3TC + NVP-treated (8.71%) and d4T + 3TC + NVP (15.24%)-treated subjects. There was little overall improvement in the functional status, and two subjects became bedridden.

The improvement in the total lymphocyte and CD4 counts is shown in Tables 3 and 4, respectively.

Table 5 summarizes the overall outcome of HAART at the end of 24 weeks.

Tables 6–8 show the statistical significance of the TLC and CD4 count. Only 49 subjects (31%) received the AZT + 3 TC + NVP regimen throughout the study.

A total of 585 adverse events related to HAART were reported at various time intervals during the study period. They included anorexia (*n* = 35, 7.4%), fatigue (*n* = 74, 15.6%), gastritis (*n* = 18, 3.8%), giddiness (*n* = 25, 5.3%), headache (*n* = 52, 11%), myalgia (*n* = 10, 2.1%), nausea (*n* = 133, 28.1%), skin rashes (*n* = 74, 15.6%), skin/nail hyperpigmentation (*n* = 23, 4.9%), vomiting (*n* = 22, 4.6%), and weakness (*n* = 71, 15%). Other adverse events included leg pain, mouth ulcers, depression (each *n* = 7, 1.5%), drowsiness and insomnia (each *n* = 6, 1.3%), palpitations and fever (each *n* = 5, 1.1%), bad dreams (*n* = 3, 0.6%), icterus (*n* = 2, 0.4%), and hair loss and itching (each *n* = 1, 0.2%). Serious adverse events included severe anemia (*n* = 14, 3%), SJS (*n* = 5, 1.1%), and hepatitis (*n* = 1, 0.2%). Nine deaths occurred during the study period and were probably due to the natural progression of the disease (*n* = 8, 1.7%) and due to LRTI, hepatitis, and acute gastroenteritis (*n* = 1, 0.2%).

Opportunistic infections occurred only in 51 study subjects (32.3%), the commonest being oral candidiasis, respiratory tract infections, and pulmonary and extrapulmonary tuberculosis, which responded to specific therapy.

HAART substitutions had to be initiated 103 times during the study period.

Concurrent medications during the HAART were used for intercurrent illnesses or for symptomatic relief of side effects and complications, only for a specific duration. The most commonly used medications were iron and B-complex preparations, H_1 blockers (cetirizine, chlorpheniramine), analgesics/non-steroidal anti-inflammatory drugs (paracetamol, diclofenac), antiemetics (metoclopramide, domperidone), an H_2 blocker (ranitidine), an anthelmintic

Table 2: Treatment outcome [*n* (%)] (based on improvement in WHO staging and clinical parameters; *n* = number of subjects)

		AZT + 3TC + NVP	d4T + 3TC + NVP	AZT + 3TC + EFV	d4T + 3TC + EFV	NA	Total
WHO clinical staging							
Baseline*	I	59 (37.34)	3 (1.9)	—	—	—	62 (39.24)
	II	62 (39.24)	1 (0.63)	3 (1.9)	—	—	66 (41.77)
	III	27 (17.09)	2 (1.27)	1 (0.63)	—	—	30 (18.99)
	NA	—	—	—	—	—	—
24 weeks	I	44 (27.85)	21 (13.29)	50 (31.65)	—	4 (2.53)	119 (75.32)
	II	1 (0.63)	—	4 (2.53)	2 (1.27)	1 (0.63)	8 (5.06)
	III	5 (3.16)	2 (1.27)	3 (1.9)	1 (0.63)	—	11 (6.96)
	IV†	1 (0.63)	—	1 (0.63)	—	—	2 (1.27)
	NA‡	—	—	—	—	18 (11.39)	18 (11.39)
Body weight							
Baseline	Mean ± SD	55.51 ± 11.97	48.16 ± 10.3	55.25 ± 8.99	—	—	55.23 ± 11.88
24 weeks	Mean ± SD	60.35 ± 13.28	55.5 ± 10.75	57.49 ± 10.89	48.33 ± 2.57	—	57.81 ± 11.93
Functional status§							
Baseline	W	133 (84.18)	4 (2.53)	4 (2.53)	—	—	141 (89.24)
	A	15 (9.49)	2 (1.27)	—	—	—	17 (10.76)
	B	—	—	—	—	—	—
	NA	—	—	—	—	—	—
24 weeks	W	49 (31.01)	23 (14.56)	55 (34.81)	2 (1.27)	5 (3.16)	134 (84.81)
	A	1 (0.63)	—	2 (1.27)	1 (0.63)	—	4 (2.53)
	B	1 (0.63)	—	1 (0.63)	—	—	2 (1.27)
	NA‡	—	—	—	—	18 (11.39)	18 (11.39)

*Subjects with baseline stage IV were not included in the study.
†Two subjects progressed to stage IV.
‡Not available for follow-up at the scheduled visits or lost to follow-up, or deceased.
§Assessed by WAB:
W: Working = Able to perform usual work in or out of the house, harvest.
A: Ambulatory = Able to perform activities of daily living, but not able to work.
B: Bedridden = Not able to perform activities of daily living.

Table 3: Treatment outcome* [*n* (%)] (based on improvement in TLC; *n* = number of subjects)

		AZT + 3TC + NVP	d4T + 3TC + NVP	AZT + 3TC + EFV	d4T + 3TC + EFV	NA	Total
Baseline	Normal	123 (77.85)	6 (3.8)	3 (1.9)	—	—	132 (83.54)
	Lymphopenia	24 (15.19)	—	1 (0.63)	—	—	25 (15.82)
	Lymphocytosis	1 (0.63)	—	—	—	—	1 (0.63)
	NA/ND†	—	—	—	—	—	—
	Mean ± SD	5,613 ± 1875	6,433 ± 840.63	4,875 ± 1381.726	—	—	5,625.94 ± 1841
	SEM	154.15	343.18	690.86	—	—	—
	CI (95%)	302.14	672.63	1,354.06	—	—	—
4 weeks	Normal	39 (24.68)	21 (13.29)	43 (27.22)	3 (1.9)	5 (3.16)	111(70.25)
	Lymphopenia	12 (7.59)	2 (1.27)	15 (9.49)	—	—	29 (18.35)
	Lymphocytosis	—	—	—	—	—	18 (11.39)
	NA/ND†	—	—	—	—	18 (11.39)	158 (100)
	Mean ± SD	5,360 ± 1723.03	5,891 ± 1181.26	5,289 ± 1857.761	6,366 ± 2983.845	—	5,441 ± 1726.59
	SEM	237.66	246.30	241.85	241.85	—	—
	CI (95%)	472.88	482.75	474.03	474.03	—	—
	Unpaired *t*-test	0.3980	0.3029	0.663647	—	—	—

*Normal, 4,000–11,000/mm^3; lymphopenia, $<$4,000/mm^3; lymphocytosis, $>$11,000/mm^3.
†NA/ND, not available/not done.

Table 4: Treatment outcome [*n* (%)] (based on improvement in CD4 count; *n* = number of subjects)

	CD4 count*	AZT + 3TC + NVP	d4T + 3TC + NVP	AZT + 3TC + EFV	d4T + 3TC + EFV	NA	Total
Baseline	<50	12 (7.59)	—	1 (0.63)	—	—	13 (8.23)
	50–100	29 (18.35)	—	1 (0.63)	—	—	30 (18.99)
	100–200	62 (39.24)	4 (2.53)	2 (1.27)	—	—	68 (43.04)
	200–350	45 (28.48)	2 (1.27)	—	—	—	47 (29.75)
	>350	—	—	—	—	—	—
	NA/ND†	—	—	—	—	—	—
	Mean ± SD	153.18 ± 66.18	179 ± 84.92	90.5 ± 51.55	—	—	152.58 ± 67.
	SEM	5.44	34.66	25.77	—	—	—
	CI (95%)	10.66	67.94	50.52	—	—	—
24 weeks	<50	1 (0.63)	—	1 (0.63)	—	1 (0.63)	3 (1.9)
	50–100	1 (0.63)	1 (0.63)	1 (0.63)	—	–	3 (1.9)
	100–200	10 (6.33)	2 (1.27)	16 (10.13)	—	1 (0.63)	29 (18.35)
	200–350	21 (13.29)	10 (6.33)	28 (17.72)	1 (0.63)	—	60 (37.97)
	>350	18 (11.39)	10 (6.33)	12 (7.59)	2 (1.27)	3 (1.9)	45 (28.48)
	NA/ND†	—	—	—	—	18 (11.39)	18 (11.39)
	Mean ± SD	296.74 ± 138.41	348.16 ± 131.14	291.88 ± 136.73	433 ± 105.69	—	307.76 ± 138.87
	SEM	19.38	26.76	17.80	61.02	—	—
	CI (95%)	37.98	52.46	34.89	119.60	—	—
	Unpaired *t*-test	<0.01	0.005	0.005	—	—	—

*Cells/mm^3.
†Not available/not done.

Table 5: Summary of treatment outcome* [*n* (%)] (*n* = number of patients)

Outcome measure	Baseline	24 weeks	% improvement†
WHO clinical stage			
I	62 (39.2%)	119 (75.3%)	+ 36.1%
II	66 (41.8%)	8 (5.1%)	-36.7%
III	30 (18.9%)	11 (6.9%)	-12.0%
IV	—	2 (1.3%)	+ 1.3%
NA‡	—	18 (11.4%)	+ 11.4%
Weight (kg)			
Mean ± SD	55.27 ± 11.88	57.81 ± 11.93	
Functional status			
Working	141 (89.2%)	134 (84.8%)	-4.4%
Ambulatory	17 (10.8%)	4 (2.5%)	-8.3%
Bedridden	—	2 (1.3%)	+ 1.3%
NA‡	—	18 (11.4%)	+ 11.4%
CD4 count (cells/mm^3)			
<50	13 (8.2%)	3 (1.9%)	–6.3%
50–100	30 (18.9%)	3 (1.9%)	–17.0%
100–200	68 (43.1%)	29 (18.4%)	–24.7%
200–350	47 (29.7%)	60 (37.9%)	+ 8.2%
>350	—	45 (28.5%)	+ 28.5%
NA/ND‡	—	18 (11.4%)	+ 11.4%
Mean ± SD	152.58 ± 67.13	307.76 ± 138.87	

*All subjects were considered for calculation based on intent-to-treat criteria.
†Indicative of the percentage of shift i.e., inclusion into/removal from the group.
‡NA/ND, not available/not done.

Table 6: Paired-sample statistics of CD4 counts and the TLC

Parameters	Mean	n*	SD	SEM
Baseline CD4	158.71	49	69.301	9.900
24-week CD4	297.57	49	140.721	20.103
Baseline TLC	5,804.08	49	1,900.873	271.553
24-week TLC	5,357.14	49	1,707.947	243.992

*Patients receiving AZT + 3TC + NVP regimen throughout the study period.

Table 7: Paired-sample correlation of CD4 counts and the TLC

Parameters	N	Correlation	Significance
Baseline and 24-week CD4	49	0.512	0.000*
Baseline and 24-week TLC	49	0.249	0.084

*$P < 0.001$ (highly significant).

(albendazole), a glucocorticoid (prednisolone), and a herbal remedy (Liv-52).

Discussion

HAART was initiated according to the NACO guidelines using a combination of three drugs, including two NRTIs and one NNRTI. PIs were not included because of their complex dosing schedule, frequent adverse effects, and drug interactions.[3–5] The initial option for all patients was AZT + 3TC + NVP. In subjects with anemia, AZT was substituted by d4T and in the event of non-availability, skin reactions, or hepatic dysfunction, or possible drug interactions, NVP was replaced by EFV.

Subjects with comorbid conditions received appropriate therapy throughout the study period without any interruption or change. None of the medications used to manage the comorbid illnesses were known to produce any clinically significant drug interactions with antiretrovirals (ARVs) used or to alter the choice of therapy.

Although there was an overall clinical improvement, there was little improvement in the body weight and functional status of the study subjects, probably because of the limited observation period of 24 weeks. However, there was good improvement in the mean CD4 count, with 28.05% of the subjects showing an increase of > 350 cells/mm^3.

Even though there was no alteration in the mean TLC at the end of 24 weeks, the number of subjects showing lymphocytosis increased from 1 (0.6%) at baseline to 29 (18.4%) after 24 weeks, probably due to concurrent infections occurring during this period and also because of improvement in the immune status. The mean CD4 count improved from 152.58 ± 67.13 at baseline to 307.76 ± 138.87 after 24 weeks. There was a significant decrease in the number of subjects with CD4 count < 200 cells/mm^3 from 111 (70.3%) at baseline to 35 (22.2%) after 24 weeks. The number of subjects with a CD4 count of 200–350 cells/mm^3 increased from 47 (30%) at baseline to 60 (38%) after 24 weeks, and in 45 subjects (28.48%) the CD4 count increased to > 350 cells/mm^3 ($P < 0.01$). Unlike reports from other studies, there was little improvement in the TLC. Other studies have reported significant improvement in subjects with a baseline CD4 count of 200–350 cells/mm^3, although with less significant improvement in those with baseline CD4 count < 200 cells/mm^3, in spite of continued therapy up to 2 years, and even with change to boosted or unboosted PI-based therapy.[6–9] This may probably be because of infection with resistant/mutant HIV strains and also because of severe opportunistic infections. There was a significant improvement of CD4 count under the AZT + 3TC + NVP regimen ($P < 0.001$), with little change in the TLC ($P = 0.084$). Only two subjects deteriorated to WHO stage IV despite improvement in CD4 count. Other studies have reported significant improvement in body weight but deterioration in WHO staging and functional status in spite of longer duration of therapy, which may probably be because of inclusion of subjects with late/advanced stages (WHO stage IV) with very low CD4 counts (< 200 cells/mm^3).[10,11] Out of 158 subjects included in the study, only 137 (86.7%) were available for follow-up monitoring at the end of 24 weeks. However, all subjects were considered for the analysis based on the intention-to-treat criteria. There was a significant clinical improvement as indicated by WHO clinical staging, but there was little improvement in the functional status.[12]

The ARVs used in the present study were generally well tolerated, producing only mild, self-limiting adverse events not requiring discontinuation of therapy, and were managed by reassurance and symptomatic therapy.

Drugs that were used to manage opportunistic infections did not have any interactive potential with the study drugs and they did not alter the ongoing course of the ART. There was no correlation between the baseline CD4 count and the

Table 8: Paired-sample *t*-test of CD4 counts and the TLC

Parameters	Paired differences					t-Test	df	Sig. (two-tailed)
	Mean	SD	SEM	95% CI of differences				
				Lower	Upper			
Baseline and 24-week CD4	–138.86	120.937	17.277	–173.59	–104.12	–8.037	48	0.000
Baseline and 24-week TLC	446.94	2,216.614	316.659	–189.75	1,083.62	1.411	48	0.165

occurrence of opportunistic infections. None of the subjects developed *Pneumocystis carinii* pneumonia (PCP) probably because of cotrimoxazole prophylaxis.

Substitutions in HAART regimen were made mainly because of intolerable adverse events or possible drug interactions with the drugs used for opportunistic infections (*n* = 40, 25.3%), or because of non-availability of the NACO-sponsored drugs (*n*=63, 40%). Twenty-six subjects (16.5%) under initial therapy with AZT-based regimen were moved to d4T-based regimen because of anemia; six subjects (3.8%) under NVP-based therapy changed to EFV-based regimen because of SJS (*n*=5, 3.2%) and hepatitis (*n*=1, 0.6%); and seven subjects (4.4%) with newly diagnosed tuberculosis were moved from NVP- to EFV-based regimen to avoid interaction with rifampicin. NVP was also substituted by EFV when the former drug was out of NACO supply. In other studies, similar patterns of HAART substitutions have been reported [13–17].

The drawbacks of the study included limited period of observation and follow-up, and exclusion of subjects with advanced stages of the disease or with severe opportunistic infections, and subjects belonging to special risk groups such as pregnant women, children, and elderly subjects ($>$65 years).

Conclusion

The present study indicates that the NACO-recommended HAART involving two NRTIs and one NNRTI has shown good efficacy in overall clinical improvement, increasing the CD4 count and preventing opportunistic infections. This is in spite of the limited observation period and follow-up of 24 weeks. The drugs showed good tolerability, with mild, tolerable, self-limiting, and controllable adverse effects. However, serious adverse events, requiring hospitalization and specific interventional therapy, also occurred. Cotrimoxazole prophylaxis has also contributed in preventing opportunistic infections like PCP.

More elaborate studies using HAART regimens other than the NACO-sponsored regimen, such as the recent WHO-recommended regimen involving FTC + TDF + EFV in OD dosing and involving subjects with advanced stages of disease from all age groups, are worth undertaking for generating more useful updated information that may further improve the quality of care.

References

1. Department of AIDS Control, Ministry of Health & Family Welfare. NACO Annual Report 2011–12. March 2012 [cited 23 March 2013]. Available from: http://www.nacoonline.org/upload/Publication/Annual%20Report/NACO_AR_Eng%202011-12.pdf
2. National AIDS Control Organization of India (NACO), May 2007. Antiretroviral therapy guidelines for HIV-infected adults and adolescents including post-exposure prophylaxis [cited 10 September 2011]. Available from: http://www.nacoonline.org
3. Sweetman SC, editor. Martindale: The complete drug reference. 36th ed. London: Pharmaceutical Press; 2009. pp. 856–951.
4. Flexner C. Antiretroviral agents and treatment of HIV infection. In: Brunton LL, Chabner BA, Knollmann BC, editors. Goodman & Gilman's the pharmacological basis of therapeutics. 12th ed. New Delhi: McGraw-Hill Publishers; 2006. pp. 1623–63.
5. Safrin S. Antiviral agents. In: Katzung BG, Masters SB, Trevor AJ, editors. Basic and clinical pharmacology. 11th ed. New Delhi: McGraw-Hill publishers; 2009. pp. 845–75.
6. Waters L, Stebbing J, Jones R, Michailidis C, Sawleshwarkar S, Mandalia S, et al. A comparison of the CD4 response to antiretroviral regimens in patients commencing therapy with low CD4 counts. J Antimicrob Chemother 2004;54:503–7.
7. Waters L, Fisher M, Anderson J, Wood C, Delpech V, Hill T, et al. Responses to highly active antiretroviral therapy and clinical events in patients with a low CD4 cell count. HIV Med 2011;12(5):289–98.
8. Babiker A, Darbyshire J, Pezzotti P, Porter K, Prins M, Sabin C, et al. Short-term CD4 cell response after highly active antiretroviral therapy initiated at different times from seroconversion in 1500 seroconverters. J Acquir Immune Defic Syndr 2003;33 (3):303–10.
9. Siegfried N, Uthman OA, Rutherford GW. Optimal time for initiation of antiretroviral therapy in asymptomatic, HIV-infected, treatment-naïve adults. Cochrane Database Syst Rev 2010;(3): CD008272.
10. Thejus TJ, Jeeja MC, Jayakrishnan T. The functional status of patients with AIDS attending antiretroviral treatment center. Indian J Palliat Care 2009;15(1):57–60.
11. Olawumi HO, Olatunji PO, Salami AK, Odeigah L, Iseniyi JO. Effect of highly active antiretroviral therapy on CD4 count and weight in AIDS patient seen at the UITH, Ilorin. Niger J Clin Pract 2008;11(4):312–5.
12. Rosen S, Larson B, Brennan A, Long L, Fox M, Mongwenyana C, et al. Economic outcomes of patients receiving antiretroviral therapy for HIV/AIDS in South Africa are sustained through three years on treatment. PLoS ONE 2010;5(9):e12731.
13. Sharma SK, Dhooria S, Prasad KT, George N, Ranjan S, Gupta D, et al. Outcomes of antiretroviral therapy in a northern Indian urban clinic. Bull World Health Organ 2010;88:222–6.
14. Dou Z, Chen RY, Xu J, Ma Y, Jiao JH, Durako S, et al. Changing baseline characteristics among patients in the China National Free Antiretroviral Treatment Program, 2002–09. Int J Epidemiol 2010;39:ii56–64.
15. Getahun A, Tansuphasawadikul S, Desakorn V, Dhitavat J, Pitisuttithum P. Efficacy and safety of generic fixed-dose combination of stavudine, lamivudine and nevirapine (GPO-vir) in advanced HIV infection. J Med Assoc Thai 2006;89(9):1472–8.
16. Agarwal D, Chakravarty J, Chaube L, Rai M, Agarwal NR, Sundar S. High incidence of zidovudine induced anaemia in HIV infected patients in eastern India. Indian J Med Res 2010;132:386–9.
17. Colebunders R, Kamya MR, Laurence J, Kambugu A, Byakwaga H, Mwebaze PS, et al. First-line antiretroviral therapy in Africa—how evidence-based are our recommendations? AIDS Rev 2005; 7:148–54.

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