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Changes in Lipid Profiles in Two Groups of HIV-1 Infected Patients in Cameroon on Two Treatment Regimens with Either Efavirenz or Nevirapine, in Association with Reverse Transcriptase Inhibitors

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The aim of this study was to determine the effect of two antiretroviral therapy regimens on lipid profiles. Patients were allocated to two treatment regimens: Nevirapine (NVP) + Stavudine (d4T) + Lamivudine (3TC) (n = 197) or Efavirenz (EFV) + Stavudine (d4T) + Lamivudine (3TC) (n = 181). Serum was prepared from blood samples collected before the start of treatment (Month 0) and at 24 months. Lipids and lipoproteins were measured using colorimetric enzyme assays or by calculation. Overall, there was an increase in all lipid parameters in patients on both treatment regimens at 24 months, although there were individual differences with respect to each lipid parameter that affected the atherogenicity indices for both regimens. Increase of high density lipoprotein cholesterol (HDLC) (42.82%) was significantly larger in patients on the NVP than on EFV (24.03%) ($p<0.001$), as opposed to Total Cholesterol (TC), triglycerides (TG) And Low Density Lipoprotein Cholesterol (LDLC) that were significantly lower in patient on NVP than on EFV; TG, Very Low Density Lipoproteins (VLDL) and LDLC increased in both regimens. These changes were not much affected by changes in viral load and CD_4 cell levels. The changes in the atherogenicity indices showed that the regimen with NVP seems to have less risk of coronary heart disease compared to EFV.

Key words: Lipid profiles, atherogenicity indices, Efavirenz, Nevirapine, HIV type 1

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INTRODUCTION

In untreated HIV infected individuals, particularly those with advanced infection, lipid abnormalities are common (Grundfeld *et al*., 1992; Feingold *et al*., 1993). Abnormalities include variations in Low Density Lipoprotein Cholesterol (LDLC) and High Density Lipoprotein Cholesterol (HDLC) levels (Feingold *et al*., 1993; Nguemaïm *et al*., 2010). Further, metabolic disorders, which include disturbances in lipid metabolism and increases in serum level of triglyceride and cholesterol, have been observed in all stages of HIV-infection (Bernasconi *et al*., 1998; Mooser and Carr, 2001; Danwe *et al*., 2005). Before the advent of Highly Active Antiretroviral Therapy (HAART), antiretroviral drugs such as zidovudine (AZT) were shown to decrease plasma triglycerides levels (Mildvan *et al*., 1992).

Combination of antiretroviral therapy (ART) for treatment of HIV type 1 infection has been associated with fat redistribution, insulin resistance and changes in plasma lipid concentrations (Mildvan *et al*., 1992; Carr *et al*., 1998, 1999, 2000; Behrens *et al*., 1999; Periard *et al*., 1999; Mulligan *et al*., 2000). More dyslipidaemia with different patterns have been observed in patients receiving protease inhibitor based HAART (Henry *et al*., 1998; Bertold *et al*., 1999; Carr *et al*., 1999; Dong *et al*., 1999; Roberts *et al*., 1999; Bonnet *et al*., 2000; Bozzette *et al*., 2003). A recent study, by Smith *et al*. (2004) demonstrated an excess of cardiovascular risk factors in HIV patients receiving HAART (Carr *et al*., 1998). Non Nucleoside Reverse Transcriptase Inhibitor (NNRTI) based regimens differ from protease inhibitor (PI) based regimens by the marked increases of LDLC and TG (Van der valk *et al*., 2001; Tashima *et al*., 2003). The NVP-containing regimen increased total-cholesterol, HDLC concentration and particle size and apolipoprotein A_1 (apo A_1) levels at 24 weeks (Clotet *et al*., 2003). Although, no clinical data have yet been generated to support this hypothesis, these differences between ART regimens raised the expectation that NNRTI-based regimens, particularly in view of their effects on HDLC, may favourably modify Coronary Heart Disease (CHD) risk compared with many PI containing regimens. In addition, patients infected with HIV initiating antiretroviral therapy (ART) containing a Non Nucleoside Reverse Transcriptase Inhibitor (NNRTI) show fewer atherogenic lipid changes than those initiating most ARTs containing protease inhibitors (Van Leth *et al*., 2004). With respect to the two most commonly used NNRTIs, NVP and EFV, no detailed comparative study has been reported in Cameroon concerning their effect on serum lipid profiles. In the present study, we analysed lipid and lipoprotein changes in two groups of HIV-1 patients on two treatment regimens, both including Stavudine (d4T) and Lamivudine (3TC) with one group containing NVP and the other EFV in order to improve the management of HIV-1 infected patients.

MATERIALS AND METHODS

Participants and treatment allocation: Patients enrolled in the present study were more than 15 years (mean 32.62) old. The main exclusion criteria were pregnancy, breastfeeding, abnormal laboratory results at screening and use of drugs which either affect the immune system or lipid parameters (Table 1). Patients took d4T (one tablet of 40 mg twice daily) and 3TC (one tablet of 150 mg twice daily). The first dose of both drugs was taken at 7 am and the second at 7 pm. In addition, patients were randomly allocated to NVP (one tablet of 200 mg twice daily at 7 am and 7 pm), or EFV (one tablet of 600 mg once daily at bedtime or one tablet of 800 mg once daily at bedtime, depending on whether they had associated opportunistic infections treatment, especially tuberculosis drugs). All the patients were Cameroonians and were recruited during the dermatology consultation at the Yaoundé University Teaching Hospital (Cameroon) from September 2007 to September 2009. The study was approved by the National Ethics Committees of the Ministry of Public Health. All patients gave a written informed consent before they were recruited.

Lipid parameters assessment: Serum samples for determination of lipids and lipoprotein parameters were collected at baseline before start (month 0) of antiretroviral treatments and at months 3,6,9,12,18 and 24 months. Blood was taken from participants after 12 h fasting in the dry tubes. After centrifugation at 3000 g for

Table 1: Sampling (eligibility and exclusion)

Sampling	No.
Assessed for eligibility	540
Excluded	162
Eligible for assays	378
Reason for exclusion of 162 participants	
Pregnancy or breastfeeding	21
Hepatitis B/C	08
Diabetes	11
Abnormal thyroid hormone	04
Hyperurecemia	04
Use of hormonal contraceptive	08
Obesity	24
Hypertension	11
Kidney disease	03
Family history of dyslipidaemia	12
Abnormal blood count	16
Smoker	13
Patient with associated exclusion criteria	27

10 mn, sera obtained were aliquoted and set aside for analysis of blood lipids. All samples were stored at -20°C and analysed within a week in the Biochemistry Laboratory of Yaounde Gynae-Obstetric and Paediatric Hospital according to predefined protocols using colorimetric enzyme methods. Total cholesterol was determined using enzymatic method (Allain *et al*., 1974) and serum triglyceride was determined as previously described by Buccolo and David (1973). The HDLC was determined using a heparin manganese precipitation of Apo B-containing lipoprotein (Warnick and Alberers, 1978) and serum concentration of LDLC was calculated using the Friedewald equation, but only when the concentration of TG was below 500 mg dL^{-1} (Friedewald *et al*., 1972). The VLDL (mg dL^{-1}) was calculated as TG/5 according to Friedewald *et al*. (1972) and the atherogenicity indices were calculated using TC/HDLC and LDLC/HDLC ratios. The Viral Load (VL) was measured at Centre Pasteur du Cameroun, Yaoundé laboratory using ultra sensitive Amplicor 1.5 (Roche Diagnostics, Basel, Switzerland) with a lower limit quantification of 50 copies mL^{-1} of blood.

Outcome measurement: The mean percentage changes of TG, TC, HDLC, LDLC, VLDL, TC/HDLC and LDLC/HDLC ratios, between baseline (Month 0) and month X after start of treatment were determined for each individual patient using the Van Leth *et al*. (2004) formula:

$$\text{Increase (\%)} = \frac{\text{Concentration at month X-Concentration at month 0}}{\text{Concentration at month 0}} \times 100$$

where, X is the time-points of follow-up after the start treatment (baseline or month 0).

Changes were analysed with respect to sex, Body Mass Index (BMI), CD_4 cell counts (<50, 50-200, >200 cells μL^{-1}) or Viral Load (VL) in $\log_{10}$ (< 2.5, 2.5 - 3.5, or > 3.5 $\log_{10}$).

Statistical analysis: All statistical calculations were done using computer programs Microsoft Excel 2003 and the software SPSS (Statistical Package for the Social Sciences, SPSS Inc., Chicago, IL, USA) version 12.0. For the differences between mean percentage changes level of parameters in the two treatment groups NVP and EFV modelled by repeated measurements were tested for the significance compared using the Student t-test. Student t-test was also used to compare the difference between the mean age and the mean of BMI in the two treatment groups NVP and EFV. Chi-square test was used to compare the percentages between the two groups of patients. Independent risk factors were assessed by multivariable analyses including the factors associated with percentage changes of all predefined variables in the treatment groups. The p-values less than 0.05 were considered statistically significant.

RESULTS

Patients: Of the 540 patients included in this study, 241 (44.63%) were allocated to the NVP treatment group and 230 (42.59%) to the EFV treatment group. Of these, 44 (27.16%) patients in NVP group, 49 (30.25%) in EFV group and 69 (42.59%) who did not start their treatment were excluded from the analysed. This resulted in a final sample size of 197 (52.12%) patients in the NVP group and 181 (47.88%) in the EFV group, making a total of 378 patients at the beginning of t he follow-up period (Table 1). A total of 22 patients (12 on NVP and 10 on EFV) disappeared during the follow-up period, leaving 356 patients at month 24.

The baseline characteristics of the patients included in this study are comparable for patients included in the two treatment regimens (Table 2).

Changes in lipids and lipoproteins: The proportional changes of the different serum lipid concentration and atherogenicity indices, over 24 months are graphically depicted in Fig. 1a (for TG), Fig. 1b (for TC), Fig. 1c (for HDLC), Fig. 1d (for LDLC), Fig. 1e (for VLDL), Fig. 1f (for TC/HDLC), Fig. 1g (for LDLC/HDLC). Changes at 24 months were compared to base line values at month zero. All changes within the treatment groups in lipid and lipoproteins concentration as well as atherogenicity

Table 2: Baseline characteristic of patients included in the study

Parameters	Patients put on NVP	Patients put on EFV	p-value between the two group of patient	Total of patients	All patients prior to exclusion
No.	197	181		378	540
Male (n)	66 (33.50)	47 (25.96)	0.239	113 (29.89)	205 (37.96)
Female (n)	131 (66.50)	134 (74.03)	0.503	265 (70.10)	335 (62.03)
Mean age (SE)	32.72 (3.38)	32.36 (3.39)	0.692	32.62 (3.39)	31.22 (2.38)
Mean of BMI (SE)	21.17 (2.21)	20.17 (2.23)	0.523	21.22 (2.17)	20.23 (2.33)
Mean of CD_4 cells μL^{-1} (SE)	160 (22)	180 (30)	0.750	170 (20)	180 (30)
CDC classification C (n)	62 (31.47)	56 (30.93)	0.935	118 (31.21)	180 (33.33)
CDC classification B (n)	114 (57.86)	80 (44.19)	0.130	194 (51.32)	250 (46.30)
CDC classification A (n)	38 (19.29)	28 (15.47)	0.412	66 (17.46)	110 (20.37)

Values in brackets indicate percentage. NVP: Nevirapine; EFV: Efavirenz; n: Number; CD4: Cluster of Differentiation 4; Cells μL^{-1}: Cells per microliter; SE: Standard error; CDC: Centers for disease control; BMI: Body mass index; A, B, C categories: Stages of the evolution of the HIV infection as classified by CDC/OMS in 1993. There was no statistically significant difference between the two groups of patients in the Table 2

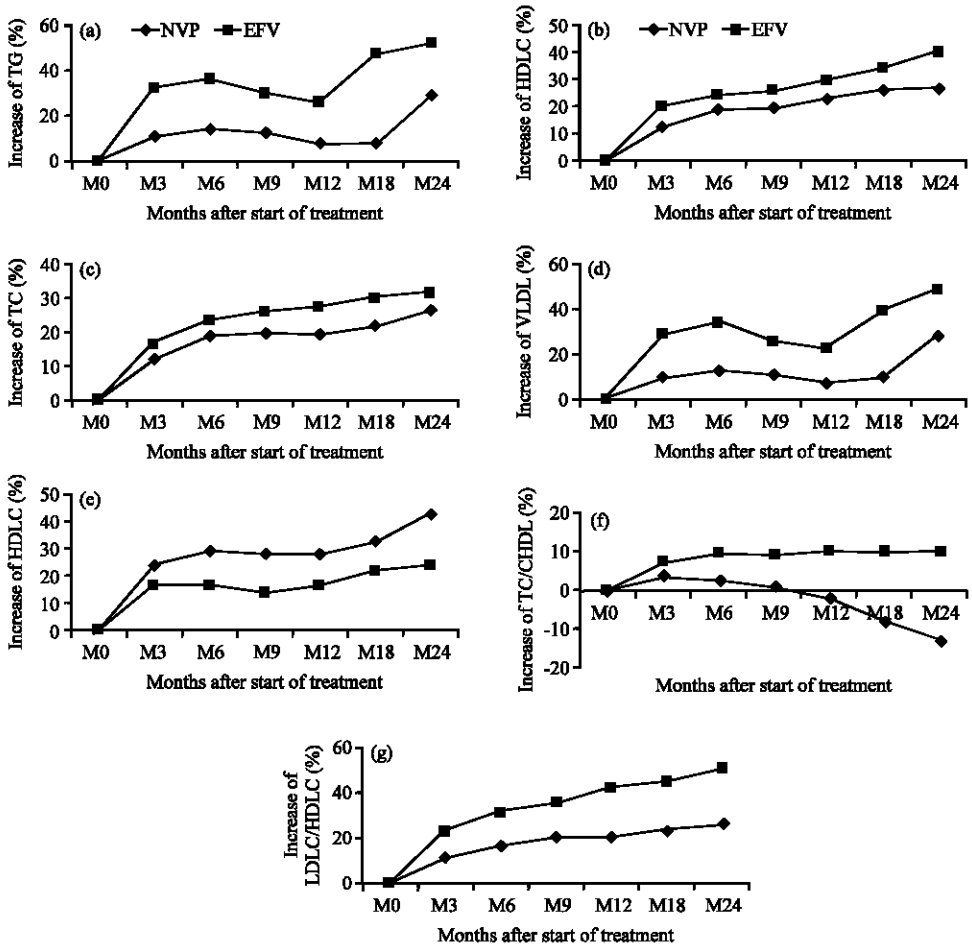

Fig. 1: Change in serum concentrations of lipids and lipoproteins

Table 3: Lipid concentrations (standard error) at baseline and 24 months and mean percentage changes

Lipid parameters and atherogenicity index	Patient taking NVP			Patient taking EFV			Difference between percent increase NVP-EFV group (95% CI)	p-value of percent increase between NVP and EFV group
	M 0 (n = 197)	M 24 (n = 185)	Percent increase	M 0 (n = 181)	M 24 (n = 171)	Percent increase		
TG (mg dL^{-1})	192.60 (5.80)	264.30 (8.25)	29.23 (1.23)	192.60 (5.82)	347.70 (9.75)	52.50 (2.69)	-23.27 (-26.62 to -15.67)	<0.001*
TC (mg dL^{-1})	278.20 (5.80)	366.02 (9.10)	26.25 (1.26)	284.21 (5.99)	386.20 (8.20)	31.57 (2.02)	-5.32 (-8.21 to -9.32)	0.043*
HDLC (mg dL^{-1})	50.78 (1.14)	87.79 (0.67)	42.82 (2.16)	53.28 (1.28)	70.33 (2.57)	24.03 (1.23)	18.79 (12.26 to 23.12)	<0.001*
LDLC (mg dL^{-1})	121.20 (3.23)	181.37 (6.23)	26.34 (1.32)	159.39 (2.78)	257.25 (6.57)	40.07 (2.72)	-13.72 (-17.32 to -6.23)	0.002*
TC/HDLC	5.61 (0.11)	4.92 (0.08)	-12.82 (0.03)	5.47 (0.14)	6.62 (0.18)	10.12 (0.82)	-22.94 (-28.13 to -16.03)	<0.001*
LDLC/HDLC	2.18 (0.08)	3.21 (0.08)	26.35 (1.25)	2.79 (0.08)	5.12 (0.12)	50.53 (3.86)	-24.18 (-31.12 to -11.14)	<0.001*
VLDL (mg dL^{-1})	38.12 (0.68)	53.74 (0.98)	29.06 (1.26)	38.32 (1.38)	69.14 (2.34)	48.62 (3.26)	-19.56 (-26.14 to -9.13)	<0.001*

M0: Month 0; M24: Month 24; n: Effective; SE: Standard error; a: Mean values of lipid parameters and atherogenicity indice (SE); b: Mean percentage change (SE) modelled by repeated measurements; CI: Confidence interval; NVP: Nevirapine; EFV: Efavirenz; TG: Triglycerides; TC: Total cholesterol; HDLC: High Density lipoprotein cholesterol; LDLC: Low density lipoprotein cholesterol; VLDL: Very low density lipoprotein; TC/HDLC and LDLC/HDLC: Atherogenicity indices; mg dL^{-1}: Milligram per decilitre; n: Number. *Statistically significant results when the percent increase in the two group of patients are compared ($p<0.05$).

indices (TC/HDLC, LDLC/HDLC ratios) were statistically significant (Table 3).

The increase of HDLC was significantly larger in the NVP treatment group (42.82%) than in EFV treatment group (24.03%) ($p<0.001$) (Table 3). In contrast, the increase in TC was significantly smaller in NVP group (26.25%) than the EFV group (31.57%) ($p = 0.043$). These changes resulted in the significant decreased of TC/HDLC ratio in the NVP group (-12.82%) compared to an increase in the EFV group (10.12%) ($p<0.001$).

The increase of TG was significantly smaller in the NVP group (29.23%) than in the EFV group (52.50%) ($p<0.001$), as well as the increase of VLDL (29.06%) in NVP group compared to 48.62% in EFV ($p<0.001$). The difference in increase of LDLC was also statistically significant (26.34% for NVP group compared to 40.07% for EFV group; $p = 0.002$) (Table 3).

Effect of sex, Viral Load (VL), Body Mass Index (BMI) and CD_4 cell counts: Some factors associated with changes in lipid concentration were analysed by a multivariable analysis (Table 4, 5). According to sex, the increase of HDLC ($p = 0.042$) and TC ($p<0.001$) was significantly smaller in women than in men (Table 4). This resulted in a greater decrease of TC/HDLC ratio for men (-9.84%) compared to women (7.14%) ($p<0.001$) (Table 5). There was a significant increase in all lipid levels and TC/HDLC ratio in patients associated with a decrease of VL over 24 months except for LDLC and LDLC/HDLC ratio whose increase was larger only when VL remained more than 2.5 $\log_{10}$. There was a significant association between VL ($\log_{10}$) and lipids, except HDLC ($p = 0.072$) (Table 4) and LDLC ($p = 0.064$) (Table 5).

The BMI was significantly associated with increase in all lipid parameters and LDLC/HDLC ratio, except TC/HDLC ratio ($p = 0.062$) (Table 5).

Table 4: Multivariable analysis of some factors associated with percentage changes in lipid (TG, TC and HDLC) concentrations (SE)

	TG (mg dL^{-1})			TC (mg dL^{-1})			HDLC (mg dL^{-1})		
Variables	M0 [a]	M24 [a]	PI [b]	M0	M24	PI	M0	M24	PI
Sex									
M	178.80 (5.60)	309.00 (9.50)	54.01 (4.06)	288.00 (9.60)	426.11 (10.85)	39.91 (2.12)	54.06 (1.22)	83.08 (1.35)	35.02 (1.42)
F	206.40 (6.02)	303.00 (8.50)	27.72 (1.98)	274.40 (6.80)	326.11 (7.35)	17.90 (1.16)	50.00 (1.20)	75.04 (0.86)	31.83 (1.12)
p-value			<0.001*			<0.001*			0.042*
BMI (kg m^{-2})									
<18.99	169.20 (4.70)	214.03 (8.40)	27.49 (1.34)	239.50 (7.26)	309.11 (7.25)	26.06 (1.12)	49.05 (0.91)	79.00 (0.94)	37.77 (1.52)
18.99-24.99	216.00 (6.92)	397,98 (9.60)	54.24 (2.58)	322.91 (9.14)	443.11 (10.95)	37.81 (2.16)	55.01 (1.51)	79.12 (1.30)	29.08 (1.02)
p-value			0.002*			0.031*			0.028*
VL $\log_{10}$									
<2.5	166.60 (5.41)	307.32 (8.36)	28.25 (1.38)	181.20 (7.20)	320.10 (8.33)	35.24 (1.78)	62.03 (1.24)	98.34 (1.31)	27.06 (1.29)
2.5-3.5	192.69 (5.30)	219.32 (9.17)	14.87 (1.09)	381.19 (10.20)	426.30 (11.43)	3.98 (0.08)	56.09 (1.24)	79.79 (1.25)	11.98 (0.71)
>3.5	218.49 (6.70)	393.34 (9.47)	38.61 (1.45)	281.19 (7.20)	381.92 (7.53)	18.65 (1.41)	38.00 (1.15)	59.05 (0.81)	27.81 (1.39)
p-value			<0.001*			<0.001*			0.072
CD_4 (cells μL^{-1})									
<200	172.30 (5.80)	275.33 (8.66)	42.89 (2.06)	300.89 (8.55)	381.88 (8.40)	35.76 (2.06)	62.06 (0.71)	79.69 (1.38)	13.57 (1.07)
200-350	212.90 (5.82)	309.32 (9.66)	38.84 (1.86)	261.51 (7.85)	291.77 (8.50)	22.06 (1.22)	42.00 (1.71)	78.54 (1.01)	53.28 (2.32)
>350		333.33 (8.67)			454.68 (10.40)			78.94 (0.97)	
p-value			0.043*			<0.001*			<0.0001**

M0: Month 0; M24: month 24; [a]: Mean values of lipid parameters and atherogenicity indice (SE); [b]: Mean percentage change (SE) modelled by repeated measurements; CI: Confidence interval; M: Male; F: Female; PI: Percent increase; SE: Standard error; BMI: Body mass index; kg m^{-2}: Kilogram per millimetre square; mg dL^{-1}: Milligram per decilitre; Cells μL^{-1}: Cells per microliter; VL: Viral load; log10: Decimal logarithm; CD4: Cluster of Differentiation 4; TG: Triglycerides; T C: Total cholesterol; HDLC: High density lipoprotein cholesterol; *statistically significant results ($p<0.05$). **Statistically higher significant results ($p<0.0001$)

Table 5: Multivariable analysis of some factors associated with percentage changes in lipid (LDLC and VLDL) concentrations (SE) and atherogenicity index (SE)

	LDLC (mg dL^{-1})			TC/HDLC			LDLC/HDLC			VLDL (mg dL^{-1})		
Variables	M0 [a]	M24	PI	M0	M24	PI	M0	M24	PI	M0	M24	PI
Sex												
M	135.30 (3.00)	204.11 (6.10)	25.48 (1.46)	5.82 (0.13)	5.38 (0.13)	- 9.84 (0.38)	1.24 (0.06)	2.18 (0.09)	46.59 (4.56)	35.55 (1.00)	62.17 (1.30)	50.01 (2.46)
F	145.30 (3.00)	234.51 (6.30)	40.93 (2.58)	5.26 (0.13)	6.16 (0.19)	7.14 (0.47)	3.72 (0.09)	5.56 (0.11)	30.29 (3.60)	40.89 (1.06)	60.71 (2.02)	27.67 (2.06)
p-value			0.031*			<0.001*			0.002*			<0.001*
BMI (kg m^{-2})												
<18.99	125.10 (2.80)	174.62 (3.28)	23.45 (1.98)	5.05 (0.10)	4.93 (0.13)	-10.76 (0.57)	2.65 (0.09)	2.99 (0.09)	25.61 (1.33)	33.24 (1.01)	43.60 (1.28)	23.56 (1.61)
18.99-24.99	155.50 (3.20)	264.00 (9.52)	42.96 (2.06)	6.03 (0.16)	6.61 (0.19)	8.06 (0.81)	2.36 (0.07)	4.76 (0.11)	51.28 (6.83)	43.20 (1.05)	79.30 (2.04)	39.52 (2.91)
p-value			<0.001*			0.062			<0.001*			<0.001*
VL $\log_{10}$												
<2.5	152.31 (3.00)	236.50 (9.80)	18.93 (1.05)	2.75 (0.08)	3.08 (0.14)	7.56 (0.46)	2.20 (0.08)	3.23 (0.09)	21.41 (3.33)	32.99 (1.00)	59.84 (1.89)	39.91 (2.49)
2.5-3.5	124.60 (3.00)	196.21 (4.80)	21.45 (1.98)	6.24 (0.17)	6.04 (0.18)	- 12.95 (0.02)	2.07 (0.08)	3.10 (0.08)	25.17 (3.72)	38.08 (1.02)	63.74 (1.51)	26.33 (4.09)
>3.5	144.00 (3.01)	225.20 (4.72)	26.03 (1.01)	7.83 (0.15)	7.98 (0.20)	2.68 (0.37)	3.17 (0.07)	5.27 (0.14)	30.30 (5.18)	43.58 (1.07)	60.76 (1.57)	11.44 (2.03)
p-value			0.064			<0.001*			0.056			<0.001*
CD_4(cells/μL^{-1})												
<200	102.51 (2.00)	163.11 (5.63)	45.30 (2.19)	4.85 (0.09)	5.59 (0.16)	12.04 (0.75)	1.82 (0.03)	2.87 (0.06)	39.65 (2.67)	34.25 (1.03)	55.44 (1.62)	49.56 (2.56)
200-350	178.09 (4.00)	194.96 (5.28)	21.11 (1.85)	6.23 (0.17)	5.65 (0.16)	-14.74 (0.10)	3.14 (0.11)	4.87 (0.14)	29.17 (2.44)	42.19 (1.24)	62.11 (1.91)	28.12 (1.78)
>350		299.86 (8.29)			6.07 (0.14)			3.87 (0.06)			66.77 (1.44)	
p–value			<0.001*			<0.001*			0.045*			<0.001*

M0: Month 0; M24: Month 24; [a]: Mean values of lipid parameters and atherogenicity indice (SE); [b]: Mean percentage change (SE) modelled by repeated measurements; CI: Confidence interval; M: Male; F: female; PI: Percent increase; SE: Standard error; BMI: Body mass index; mg dL^{-1}: Milligram per decilitre; Cells μL^{-1}: Cells per microliter; VL: Viral load; CD4: Cluster of differentiation 4; LDLC: Low density lipoprotein cholesterol; VLDL: Very low density lipoprotein; TC/HDLC and LDLC/HDLC: Atherogenicity indices; kg m^{-2}: Kilogram per millimetre square; log10: Decimal logarithm. *Statistically significant results ($p<0.05$)

The CD_4 cell counts were in general, positively associated with changes in lipid parameters and in atherogenicity indices (Table 4, 5).

DISCUSSION

Initiation of an ART regimen containing NVP or EFV is accompanied by a significant increase of HDLC with concomitant increases of TG, TC, LDLC and VLDL. The increase of HDLC was significantly larger in the NVP treatment group compared to the EFV treatment group as well as the increase of TG, TC, LDLC and VLDL. In the NVP group, the TC/HDLC and LDLC/HDLC ratios decreased, compared to an increase in the EFV group. These observations are different from reported changes in most PI-based ART regimens, in which higher concentration of TC, LDLC and TG were found without concurrent higher levels of HDLC (Stein *et al*., 2003; Fontas *et al*., 2004) they also differ from the results of Nunez *et al*. (2002) that did not show any differences between NVP and EFV treatment groups. Present findings agree with those of Van Leth *et al*. (2004), who used cases from many countries, including African countries.

HDLC increase and NNRTIs: Present results showed an increase of HDLC in both treatment groups at 24 months. Increase of HDLC with the use of NVP or EFV have been described in some previous studies, in patients switching from a PI-based regimen to a NNRTI-based regimen (Martinez *et al*., 1999; Negredo *et al*., 2002), for patients initiating treatment with Didanosine, Stavudine and NVP (Van der valk *et al*., 2001), in patients treated with EFV and either Zidovudine with 3TC or Indinavir (Tashima *et al*., 2003) in treatment-naive subjects receiving NVP in combination with the nucleoside analogues Zidovudine/Lamivudine (Fisac *et al*., 2004) and in naive patient starting a regimen of Didanosine, d4T and EFV (Negredo *et al*., 2002). Apart from the study by Negredo *et al*. (2002) which included patients with similar baseline HDLC levels as in the present study and which showed increases in HDLC similar to the ones we report here, the others showed different increase patterns, probably due to differences in viral load, the PI-based regimen and the degree of strict adherence of the patients to the treatment protocol. Further, Riddler *et al*. (2003) also reported similar variations to ours for TC and LDLC.

Several studies have shown that an HDLC increase is associated with a significant decrease in mortality from Coronary Heart Disease (CHD) independent of changes in LDLC (Manninen *et al*., 1988; Rubins *et al*., 1999). Other studies have associated risk of cardiovascular disease (CVD) with low concentrations of HDLC (Lipid Research Clinics Program, 1984; Frick *et al*., 1987; Castelli, 1988; Gordon *et al*., 1989; Assmann *et al*., 1996; Robins, 2001). Taken together, our results show that the NVP regimen leads to lower atherogenicity index and so reduces CHD risk better than the EFV regimen. Other studies have shown that a substitution of IP with Nevirapine in combination of antiretroviral therapy for 6-12 improved and even normalized dyslipidemia, glycemia and insuline resistance, whereas HIV suppression was maintained (Molina *et al*., 2000; Moyle *et al*., 2001).

Changes in TG, TC, LDLC, VLDL and atherogenicity indices: Present results show that EFV causes a greater increase in TG levels than NVP. These results corroborate those of other authors (Molina *et al*., 2000; Negredo *et al*., 2002; Fisac *et al*., 2004). The results are unlikely to be explained by the effect of d4T, since the proportion of patients in both groups on d4T was virtually the same (52.12% for the NVP treatment group and 47.88% for the EFV treatment group). The d4T might however be responsible for the apparent acceleration of the increase of TC and TG towards the end of the study (Fig. 1), probably related to the lipodystrophy reported in patients on d4T treatment (Heath *et al*., 2001; Dube *et al*., 2002; Nolan *et al*., 2003; Sattler, 2003; Nolan and Mallal, 2004; McComsey *et al*., 2004) and the possible association of HIV-1 infection with the reduced TG clearance following food intake (Grundfeld *et al*., 1992). Concentration of TG had an effect in the calculated values of LDLC and VLDL; however, the smaller increase in levels of LDLC and TG in the NVP regimen than for the EFV might suggest that the LDLC and TG results are valid. Furthermore, elevated cholesterol has been observed with the use of EFV (Martinez *et al*., 1999) and NRTIs such as Stavudine (d4T) (Mallal *et al*., 2000). A great improvement of atherogenicity indices (TC/HDLC and LDLC/HDLC) on NVP compared to EFV was observed and this result correlates those of Ngondi *et al*. (2007). The low atherogenicity indices can be explained by the reduction of TC, LDLC and the elevation of HDLC on NVP.

CONCLUSION

The HDLC increases were higher in patients on the NVP regimen than those on the EFV regimen. The increase of TG, TC, LDLC and VLDL levels are smaller for patient taking NVP than for those taking EFV. The less atherogenic lipid profile of patients taking NVP in comparison to those taking EFV may be among the various factors to consider when selecting the most appropriate initial ART regimen, particularly for those patients with HIV type 1 with a significant a priori CHD risk like diabetes, or a previous cardiovascular event.

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