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Dyslipidemia and Adherence to the Mediterranean diet in Croatian HIV-infected Patients during the First Year of Highly Active Antiretroviral Therapy

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Abstract

We investigated the association of adherence to the Mediterranean diet and other risk factors for dyslipidemia in HIV-infected Croatian patients during the first year of highly active antiretroviral therapy (HAART). Adherence to the Mediterranean diet was determined by a 150-item questionnaire; a 0 to 9-point diet scale was created that stratified respondents as having low adherence (<4 points) and moderate to high adherence (≥ 4 points). We interviewed 117 participants between May 2004 and June 2005 and abstracted their serum lipid measurements taken during the first year of HAART. The values of total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides increased most prominently in the first 3 to 6 months after initiation of HAART (average increase at 3 months: 25% for total cholesterol, 22% for LDL-cholesterol, 18% for HDL-cholesterol and 43% for triglycerides). A Mediterranean diet and physical activity had no effect on serum lipids. The mean total cholesterol was higher in participants receiving a combination of a non-nucleoside reverse transcriptase inhibitor and a protease inhibitor compared to participants receiving a combination of nucleoside analogs with a non-nucleoside analog or a combination of nucleoside analogs and a protease inhibitor. Among individual drug treatments, indinavir/ritonavir had the most unfavorable lipid profile. We conclude that adherence to a Mediterranean diet does not influence serum lipid profiles during the first year of HAART.

Keywords

dyslipidemia; HIV; HAART; Mediterranean diet; physical activity

Introduction

Abnormalities in lipid metabolism have been reported among patients infected with the human immunodeficiency virus (HIV) even before the introduction of highly active antiretroviral therapy (HAART)[1–3]. Elevated levels of triglycerides and decreased total cholesterol and HDL-cholesterol have been shown to be positively correlated with the progression of HIV infection and have become a common finding in AIDS1.

Results of cross-sectional and longitudinal studies reported dyslipidemia in participants treated with all three drug classes, including protease inhibitors (PI)[4–9], nucleoside reverse transcriptase inhibitors (NRTIs)[10,11], and non-nucleoside reverse transcriptase inhibitors (NNRTI)[11–15]. Changes in lipid metabolism due to treatment with these drugs include

increases in total cholesterol[6,9,16], high-density lipoprotein (HDL)-cholesterol[17–21], low-density lipoprotein (LDL)-cholesterol[16,22–24], and triglycerides[17,25].

We have previously reported that moderate to high adherence to the Mediterranean diet was associated with a lower risk of clinical lipohypertrophy in 136 Croatian HIV-infected patients on HAART[26]. Non-smokers who at least moderately adhered to the Mediterranean diet had a lower risk of clinical lipoatrophy[26]. The purpose of this study was to estimate the magnitude of lipid changes and identify risk factors that influence lipid metabolism during the first year of HAART. We were specifically interested in whether adherence to the Mediterranean diet was associated with fewer lipid alterations in Croatian patients.

Patients and Methods

Study population

The present report includes 117 of 136 participants from the study on the effect of the Mediterranean diet on body shape changes during HAART because baseline (prior to HAART) lipid measurements were not available for 19 participants. We assessed body shape changes and adherence to the Mediterranean diet between May 2004 to June 2005. We abstracted data on lipids and other biochemical measurements from the electronic database of the Outpatient HIV/AIDS Department at the University Hospital for Infectious Diseases in Zagreb, Croatia which provides centralized care for all HIV-infected patients[27]. We included measurements taken from July 1997 to May 2005.

Inclusion and exclusion criteria

Male or female outpatients were eligible for study if they were older than 18 years of age, had documented HIV infection, had received HAART for at least one year, and had serum lipid measurements before start of HAART available. We excluded participants if they had uncontrolled opportunistic infections or disseminated malignancies or were pregnant or breast feeding.

Dietary assessment

We assessed adherence to the Mediterranean diet through a 150-item, interviewer-administered semi-quantitative food-frequency questionnaire provided by Antonia Trichopoulou[28] and translated into Croatian. For each of the items in the questionnaire, subjects reported frequency of consumption and portion size, and the average monthly intake was divided into daily portions. To assist in accurate determination of portions, we provided 76 photographs depicting typical portion sizes. We divided items into 12 food groups: potatoes, vegetables, legumes, fruit and nuts, dairy products, cereals, meat, poultry, fish, olive oil, eggs and alcoholic beverages. For each participant, intake of each of the indicated groups in grams per day and total energy intake were calculated. Potatoes were added to the cereal group and poultry was combined with meat to form single categories. We also calculated the ratio of monounsaturated fats to saturated fats. We used the 10-point Mediterranean diet scale developed by Trichopoulou A. et al[28] to determine dietary influence. For each subject, a value of 0 or 1 was assigned for each of the nine components of the Mediterranean diet instrument. We used the gender-specific median consumption value as the cutoff point in each food category. For the six beneficial categories (vegetable, legumes, fruits and nuts, cereal, fish and monounsaturated fat to saturated fat ratio) we assigned a value of 0 to subjects who consumed an amount below the median. For the two animal protein categories (meat plus poultry, and dairy), a value of 1 was assigned to subjects who consumed an amount below the median for each of these categories. For ethanol consumption, we assigned a value of 1 to men who consumed ≥10 grams per day and to women who consumed ≥5 grams per day. The Mediterranean diet score ranged from 0 to 9, with higher scores indicating greater adherence to the traditional Mediterranean diet.

Because of the small number of participants in our study, we dichotomized the Mediterranean diet score into below the median (<4 points, indicating low adherence to the Mediterranean diet) and at or above the median (≥4 points, indicating moderate to high adherence to the Mediterranean diet).

Energy expenditure

Energy expenditure was assessed through the seven-item International Physical Activity Questionnaire[29], translated into Croatian. This questionnaire measures self-reported physical activity. The information collected on the time spent walking, in moderate intensity and vigorous activity was used to estimate total weekly physical activity. We estimated physical activity using a weighted energy coefficient, the metabolic equivalent (MET). One MET-minute score is defined as the number of calories that a 60 kg person spends during calm sitting. For any kinds of walking we used 3.3 METs, for moderate physical activity we used 4 METs, and for vigorous physical activity we used 8 METs. We multiplied the MET value by the time spending on each of these activities. We expressed total physical activity was in minutes per week and recalculated it in hours per days.

Biologic measures

We measured plasma total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides by standard enzymatic techniques and HIV RNA level using the Amplicor Monitor RT-PCR assay (Roche Molecular Systems) with lower limit detection of 50 or 400 copies/ml. We performed CD4 lymphocyte counts by flow cytometry.

Follow up of participants

Participants generally reported for evaluation six times over the first year of treatment with HAART, and they had blood samples drawn at each visit by nursing staff. The first visit was the baseline assessment before initiation of therapy. Follow-up visits were at one month (range 15 to 60 days), three months (range 61 to 150 days), six months (range, 151 to 240 days), nine months (range, 241 to 330 days) and 12 months (range, 331 to 422 days).

Variables

The outcome variables were serum total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides, which we assessed at every visit. The principal predictor variable was adherence to the Mediterranean diet. We modeled antiretroviral treatment as a time-dependent variable. We recorded the use of each individual antiretroviral drug and antiretroviral class of drugs. Other variables included in the crude or multivariate analyses were age, gender, HIV risk behavior (heterosexual sex, men having sex with men, or other [injection drug use, hemophiliacs and unknown]), year of starting HAART, history of AIDS-defining illnesses, presence of lipodystrophy, baseline hemoglobin, plasma viral load, CD4 cell count, smoking status, energy expenditure, olive oil consumption and alcohol intake. We dichotomized plasma viral load at 400 copies/ml, baseline CD4 count at 50 or 200 cells per mm^3, and baseline hemoglobin at the median (>123 g/L). We categorized olive oil intake as yes and no, and compared moderate alcohol consumption (≥10 g/day) to no intake (<10 g/day) and no smoking to current/former smoking. We assessed clinical lipoatrophy and lipohypertrophy subjectively by participants and physicians as previously described[30] and expressed total physical activity in hours per day dichotomized at the median (>9.3 MET/h/d).

Statistical analysis

We describe our data with frequencies, medians, and interquartile ranges. The McNemar test was used to compare dichotomized lipid measurements at baseline with those at 12 months. We assessed the correlation between hemoglobin and total cholesterol with Pearson's

correlation coefficient. We log-transformed the values of triglycerides for analysis due to non-normal distribution and examined changes in mean total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides graphically over time. The crude analyses included measurements of lipids over time against one independent variable. In the multivariate model we added the principal predictor (adherence to the Mediterranean diet over time) and those variables with a level of $p \leq 0.25$ in crude analyses. We performed repeated measures of analysis of variance using the unstructured covariance matrix parameterization and explored the validity of models by graphical presentation of the residuals. We compared the results over time as the percentage of difference between categories with corresponding 95% confidence intervals and used Proc Mixed, SAS, version 9.13 (SAS Institute, Cary, NC, U S A) for our analyses.

Results

Characteristics of the study population

A total of 117 participants (males: 96, 82%) were included in the study. There were 696 measures of total cholesterol, 676 measures of HDL-cholesterol, 613 measures of LDL-cholesterol, and 696 measures of triglycerides. The main demographic and clinical characteristics are presented on Table 1. The values of total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides increased most prominently in the first 3 to 6 months after initiation of HAART (average increase at 3 months: 25% for total cholesterol, 22% for LDL-cholesterol, 18% for HDL-cholesterol and 43% for triglycerides). At baseline we observed a total cholesterol level >5 mmol/l in 21 (18%) participants, an HDL-cholesterol level >1 mmol/l in 33 (28%), an LDL-cholesterol level >3 mmol/l in 33 (28%), and a triglyceride level >1.7 mmol/l in 52 (44%) participants. After 12 month of HAART treatment, we found total cholesterol >5 mmol/l in 74 (64%) participants ($p<0.001$), HDL-cholesterol >1 mmol/l in 54 (47%) ($p<0.002$), LDL-cholesterol >3 mmol/l in 65 (56%) ($p<0.001$), and triglycerides >1.7 mmol/l in 74 (64%) ($p<0.001$).

We assessed that 78 (67%) of participants adhered moderately or highly to the Mediterranean diet. Participants with adherence to the Mediterranean diet did not differ from those without adherence with respect to the following baseline total cholesterol, HDL-cholesterol, LDL-cholesterol, or triglycerides. Among the 117 HIV-infected participants, 73 (62%) were exposed to the combination of two nucleoside reverse transcriptase inhibitors (NRTI) plus a protease inhibitor (PI), 30 (26%) to the combination of two NRTIs plus a non-nucleoside reverse transcriptase inhibitor (NNRTI), and 14 (12%) exposed to the combination of one NNRTI plus one PI.

Dietary assessments and energy expenditure

There was no statistically significant difference between serum lipid level and adherence to the Mediterranean diet based on dichotomized Mediterranean diet score. The mean difference in total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides between those who did not adhere to those who adhered to the Mediterranean diet was 0.1% (95% CI -1.5 to 1.6; $p=0.975$), 1.5% (95% CI -1.0 to 3.7; $p=0.778$), -3.9% (95% CI -6.6 to -1.5; $p=0.460$), -11.9% (95% CI -19.1 to -6.4; $p=0.256$) respectively. Olive oil consumption was also not associated with decreased lipids level. Seventy-four (63%) participants reported low-to-moderate (median 13.5 g/day) olive oil intake. Moderate ethanol intake had no effect on serum total cholesterol, LDL-cholesterol, and triglyceride level. Participants who consumed moderate amounts of ethanol (≥10 g/d) had less HDL-cholesterol than those with less or no ethanol intake (Table 2). There was no statistically significant difference between serum lipid level and energy intake.

Factors related to lipid changes

In the multivariate analysis, we found that age >39 years, heterosexual transmission, baseline hemoglobin >123 g/l, smoking or former smoking, treatment with NNRTI plus PI, and use of stavudine and indinavir/ritonavir were associated with higher levels of cholesterol (Table 2 and 3). Viral load >400 copies/ml was associated with lower levels of total cholesterol (Table 2). Hemoglobin levels were inversely correlated with total cholesterol levels; i.e. participants with lower levels of hemoglobin had lower level of total cholesterol ($p<.001$). Higher levels of HDL-cholesterol were associated with a baseline CD4 cell count >50 cells/mm^3, while male gender, use of indinavir, and indinavir/ritonavir were associated with lower levels HDL-cholesterol (Table 2 and 3). Factors related to levels of LDL-cholesterol were similar to those found for total cholesterol (Table 2 and 3). In crude analyses, triglyceride levels were significantly higher in participants treated with the combination of two NRTIs plus PI compared to participants treated with two NRTIs plus one NNRTI (-27.1%, 95% CI -35.9-20.1%, $p<0.005$). Treatment with indinavir/ritonavir (-40.4%, 95% CI -43.1-36.3%, $p<0.001$) increased the level of triglycerides most among the various treatments.

In the multivariate analysis, participants treated with two NRTIs plus PI combination had higher triglycerides levels than participants treated with two NRTIs plus NNRTI (Table 4). The use of indinavir/ritonavir was associated with highest levels of triglycerides (Table 4).

Discussion

We found no association between plasma lipid changes during the first year of HAART and adherence to the Mediterranean diet. This is similar to the non-HIV infected population where adherence to the Mediterranean diet does not correlated well with levels of serum lipids[31]. It is believed that the protective effects of the Mediterranean diet are not related to serum concentrations of total, LDL, or HDL-cholesterol but rather to changes observed in plasma fatty acids[32]. Controlled feeding studies have shown that the Mediterranean diet, where monounsaturated and polyunsaturated intake was relatively high, largely from olive oil, did reduce LDL-cholesterol and triglycerides and increased HDL-cholesterol[33]. In a randomized trial for management of hypercholesterolemia in patients on PI-containing HAART, pravastatin and dietary advice lowered cholesterol levels, whereas dietary advice alone had no effect on lipid levels[34].

We also did not find an association between adherence to the Mediterranean diet and energy intake or a correlation between plasma lipids and energy intake. There also appeared to be no beneficial effect of physical activity on lipid levels. Recent clinical trials have not demonstrated a consistent change in lipid levels in patients undertaking aerobic exercise[35,36]. Earlier clinical trials showed a beneficial effect of exercise on lipids levels in HIV infected persons treated with HAART[37–39]. We found, as others have, a significant increase in lipids after initiation of HAART[9,17,18,21,40,41]. This increase was most prominent during the first three months of therapy[17,21,41].

The most frequent NNRTI plus PI combinations used in our study were lopinavir/ritonavir plus efavirenz or indinavir plus efavirenz. Similarly to other larger multicenter cohort studies, participants treated with a NNRTI plus PI combinations had more pronounced elevations of total cholesterol compared to patients taking two NRTIs plus NNRTI and two NRTIs plus PI[14,42].

The two most commonly used NRTIs in our study were stavudine and zidovudine. Treatment with stavudine was associated with increased total cholesterol compared with zidovudine and this has also been previously described[11,43]. In earlier studies stavudine was rarely changed, because PIs were believed to cause lipid elevations[44,45]. Because of the association with

lipoatrophy, stavudine is today seldom used as first-line nucleoside treatment in developed countries[46], but it is still used in developing countries with limited choices of antiretroviral drugs[46–48].

We also confirmed that older age is associated with higher levels of total cholesterol and LDL cholesterol (Table 2)[11,14,49,50]. Participants with lower levels of baseline hemoglobin (<123 g/l) were more likely to have lower levels of total cholesterol and LDL-cholesterol. This might be a reflection of the more severe HIV disease in participants with lower hemoglobin levels. Also, baseline low levels of CD4 cells (<50 cells/mm^3) in serum were associated with lower HDL-cholesterol concentrations and this has also been previously reported[14,51,52]. A detectable viral load of >400 copies/ml of HIV RNA was most probably a result of non-adherence, so it is not surprising that it was associated with lower levels of total cholesterol as suggested by Friis-Moller et al[14].

Prevalence of smoking or former smoking was high (67%; current smokers, 49%) in our study population. However, current smoking was lower in our study population compared to findings from Italy (60%)53, Swiss (57%)54, and Norway (54.5%)55. Smoking or former smoking was associated with higher levels of total cholesterol and LDL-cholesterol. However, the association was not strong and there is no clear explanation for this observation.

Limitations of the study should be noted. Patients are instructed to come to routine visits at our outpatient HIV/AIDS Center in a fasting state. However, this is not always the case and there were no records in our database on the fasting status. This might have affected some of our results, particularly the levels of LDL-cholesterol and triglycerides. There was also a relatively large time span (from July 1997 to May 2004) when HAART was initiated. Since the interview about adherence to the Mediterranean diet took place from May 2004 to June 2005 some of the patients might have changed their diet since they started of HAART. However, our findings of the relationship between various HAART regimens and individual antiretroviral drugs are very consistent with previous reports.

This study provides important information on lipid changes and factors associated with their increase during the first year of HAART in Croatian patients. It should be noted that the benefits of Mediterranean diet in terms of survival are beyond the changes in lipids. Further studies are needed to evaluate whether adherence to the Mediterranean diet of HIV infected patients treated with HAART is beneficial in terms of prolonged survival.

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Table 1

BASELINE CHARACTERISTIC OF 117 HIV PARTICIPANTS AT THE FIRST LIPIDS MEASUREMENT

Characteristics	N or median	Percentage or interquartile range
Age, years	38.8	32.5–46.2
Male gender	96	82.1
HIV transmission		
MSM	52	44.4
Heterosexual	44	37.6
Intravenous drug use	12	10.3
Blood/blood product recipient	3	2.6
Unknown	6	5.1
Smoking (current or former)	79	68
Year of beginning treatment		
≤1999	36	30.8
2000–2001	35	29.9
≥2000	46	39.3
AIDS diagnosis	56	47.9
Viral load (copies/ml)	209 000	74 604– 640 000
CD4 count (cells/mm^3)	85	30–201
Weight (kg)	76	64–83
Body Mass Index	23.9	21.6–26.1
Hemoglobin g/l	123	110–138
Lipids (mmol/l)		
Cholesterol	4.1	3.6–4.8
HDL-cholesterol	0.9	0.6–1.1
LDL-cholesterol	2.5	2.0–3.2
Triglycerides	1.6	1.2–2.0
Initial HAART		
NNRTI + PI	14	12
Two NRTIs + NNRTI	30	25.6
Two NRTIs + PI	73	62.4

NNRTI – nonnucleoside reverse transcriptase inhibitor.
PI – protease inhibitor.
NRTIs – nucleoside reverse transcriptase inhibitors.
MSM– men who have sex with men.
HAART– highly active antiretroviral therapy.

Table 2

RELATIONSHIP BETWEEN PATIENTS CHARACTERISTICS AND CHANGE IN SERUM TOTAL CHOLESTEROL, HDL-CHOLESTEROL, LDL-CHOLESTEROL LEVEL IN 117 PARTICIPANTS, MULTIVARIATE ANALYSIS

	Total cholesterol			HDL-cholesterol			LDL-cholesterol		
Characteristics	**Estimate**	**95% Conf. interval**		**Estimate**	**95% Conf. interval**		**Estimate**	**95% Conf. interval**	
Age >39, years	−9.2% [a]*	−9.4%	−9.0%				13.0% [a]*	−13.4%	−12.6%
Gender, male	2.8%	−1.0%	6.2%	15.8%*	12.0%	19.0%	−6.4%a	−14.2%	0.2%
HIV transmission category									
Heterosexuals vs. other	−9.6%*	−13.0%	−6.7%				10.9%	−16.1%	−6.5%
Homosexuals vs. other	−7.6%	−9.8%	−5.7%				13.3%*	17.4%	−9.9%
Aids defining diagnosis				−2,3%	−2.5%	2.1%			
Lipoatrophy				9.0%	8.2%	9.9%			
Lipohipertrophy				10.3%	9.5%	11.3%			
Viral load (>400 copies/ml)	5.1%*	4.6%	5.7%						
CD4 count >200 cells/mm^3	−2.5%	−2.8%	−2.1%				−6.8%	−7.0%	−6.7%
CD4 count >50 cells/mm^3				−14.1%*	−16.8%	11.8%			
Hemoglobin >123 g/l	−10.2%*	−10.7%	−9.6%				12.7%*	−13.1%	−12.1%
Mediterranean diet	−0.9%	−2.2%	−0.2%	0.7%	−1.5%	2.5%	−6.6%	−9.0%	−4.6%
Ethanol ≥10 g/d vs. <10 g/d				18.2%*	14.1%	23.3%			
Smoking	−6.8%*	−8.3%	−5.4%				11.3%*	−14.5%	−8.7%
Treatment									
NNRTI+PI vs. two NRTIs+NNRTI	−10.5%*	−10.9%	10.0%	5.6%	1.8%	10.6%	−1.9%	−4.1%	0.9%
NNRTI+PI vs. two NRTIs+PI	−8.8%*	−10.0%	−7,5%	0.7%	−4.1%	7.1%	−3.4%	−6.3%	0.4%

[a] Variable had time interaction and results at twelve month are presented.

* Parameters were statistically significacant (P<0.05).

NNRTI – nonnucleoside reverse transcriptase inhibitor, NRTIs – nucleoside reverse transcriptase inhibitors, PI – protease inhibitor.

The characteristics +/− the percentage gives the value of the variable without the given characteristics.

Table 3

RELATIONSHIP BETWEEN ANTIRETROVIRAL DRUGS AND CHANGES IN SERUM TOTAL CHOLESTEROL, HDLCHOLESTEROL, LDL-CHOLESTEROL LEVEL, MULTIVARIATE ANALYSIS

	Total cholesterol[a]			HDL-cholesterol[b]			LDL-cholesterol[c]		
Drug	**Estimate**	**95% CI**		**Estimate**	**95% CI**		**Estimate**	**95% CI**	
Zidovudine	13.4%[d] *	12.8%	14.0%	−2.2%	−2.8%	−1.5%	12.1%[d] *	11.7%	12.6%
Stavudine	−6.8%[d] *	−7.5%	−6.0%	6.1%	5.5%	6.9%	−9.4%*	10.5%	−8.2%
Lamivudine	1.6%	0.2%	3.2%	−8.7%	−14.4%	−3.1%	1.7%	−1.3%	4.2%
Efavirenz	−1.7%	−1.8%	−1.6%	2.2%	1.1%	3.6%	2.0%[d]	1.1%	3.0%
Indinavir	0.4%	−0.5%	1.4%	35.0%[d]*	27.0%	45.8%	−0.8%[d]	−2.5%	1.3%
Indinavir/Ritonavir	−22.1%[d] *	−23.6%	20.3%	16.9%*	10.2%	25.7%	−8.3%	10.7%	−5.3%
Lopinavir/ritonavir	3.4%	−0.7%	6.5%	−10.4%	−13.8%	−6.2%	7.9%	3.2%	14.1%

[a] Adjusted for time, age, gender, HIV transmission, viral load, CD4 lymphocytes, hemoglobin, smoking, Mediterranean diet and one particular drug.

[b] Adjusted for time, gender, AIDS diagnosis, lipoatrophy, lipohypertrophy, CD4 count >50 cells/mm^3, ethanol consumption, Mediterranean diet and one particular drug.

[c] Adjusted for time, age, gender, HIV transmission, CD4 count >200 cells/mm^3, hemoglobin, smoking, Mediterranean diet and one particular drug.

[d] Variable had time interaction. The results at 12 months are presented.

* Parameters were statistically significant (P<0.05).

The characteristics +/− the percentage gives the value of the variable without the given characteristics.

Table 4

RELATIONSHIP BETWEEN VARIABLES AND PARTICULAR ANTIRETROVIRAL DRUGS AND CHANGE IN SERUM TRIGLYCERIDE LEVEL, MULTIVARIATE ANALYSIS

Variables[a]	Estimate	95% Confidence interval	
Gender male	−11.8%	−25.2%	2.0%
CD4 count >200 cells/mm3	19.8%	12.0%	33.1%
Mediterranean diet	−9.4%	−16.2%	−4.5%
Treatment			
NNRTI+PI vs. two NRTIs +NNRTI	−26.7%	−28.6%	25.7%
two NRTIs+PI vs. two NRTIs +NNRTI	−26.9%*	−36.1%	−20.4%
Antiretroviral drugs[b]			
Zidovudine	27.0%[c] *	23.1%	33.2%
Stavudine	−19.0%[c]	−19.4%	−18.5%
Lamivudine	−14.7%	−26.7%	−6.1%
Efavirenz	17.6%	13.4%	24.2%
Indinavir	43.5%*	26.3%	78.1%
Indinavir/Ritonavir	−42.7% [c] *	−44.3%	−40.3%
Lopinavir/ritonavir	−6.7%	−13.2%	4.5%

[a] Included in the model: time, gender, CD4 count >200 cells/mm^3, Mediterranean diet and type of antiretroviral treatment.

[b] Included in the model time, gender, CD4 count >200 cells/mm^3, Mediterranean diet an the particular drug.

[c] Variable had time interaction. The result from the measurement at twelve months is shown.

* Parameters were statistically significant (P<0.05).

NNRTI – non-nucleoside reverse transcriptase inhibitors, NRTIs – nucleoside reverse transcriptase inhibitors, PI – protease inhibitor.

The characteristics +/− the percentage gives the value of the variable without the given characteristics.