

EFFECTS OF DIETARY INTERVENTION ON LIPIDS PROFILE OF HIV INFECTED PATIENTS ON ANTIRETROVIRAL TREATMENT (ART)

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Abstract

The aim of this study was to evaluate the effects of dietary intervention on serum lipids, saturated fatty acids and trans-fatty acids in HIV-infected individuals on ART. This design was a non-randomized, non-controlled nutrition intervention study. The setting was in Referral Center in Infectious and Parasitic Diseases. Subjects: 57 HIV-infected patients, aged 28.4–68.4 years, were recruited from the outpatient clinic of a reference center. Clinical and

biochemical data were collected from all before and after nutritional counseling. The majority of patients were male, with at least 8 years of schooling and 38.5% had BMI \geq 25 kg/m². Forty-eight (84%) patients had a family history of chronic diseases and the most common were coronary events (50%). All patients were exposed to antiretroviral therapy and 51% were using Protease Inhibitor. Twelve patients (21%) had a very low HDL-cholesterol and 26 patients (45.5%) had hypertriglyceridemia. There were a significant increase in carbohydrate (p=0.02), protein (p=0.04), selenium (p<0.00005), and calcium (P=0.0007) intake and a significant decreased in total lipid (p=0.002), saturated fatty acids (p=0.0004), trans fatty acids (p=0.0005), and cholesterol total (p=0.0004) after dietary intervention. No significant difference was observed in energy, total fiber, polyunsaturated fatty acids and monounsaturated fatty acids after dietary intervention. This study suggested an efficacy of nutritional intervention in the prevention of changes in lipid profile of HIV-positive individuals on ART. These findings also suggest that nutritional intervention should be considered for all patients on ART.

Keywords: HIV infection, ART, dietary intervention, lipid profile

Introduction

Since the advent of the antiretroviral therapy (ART) in the mid-1990s, it has been accompanied by an important decline in mortality and morbidity associated with Human Immunodeficiency Virus (HIV) infection (Hogg *et al.*, 1997; Palella *et al.*, 1998 and Mocroft *et al.*, 1998). However, the benefits of ART are often accompanied by a substantial degree of long-term side effects that include dyslipidemia, insulin resistance, overt type 2 diabetes mellitus and changes in fat distribution, characterized by loss of peripheral deposits and/or accumulation of visceral adiposity (Carr, 2000; Guimarães *et al.*, 2007 and Guimarães *et al.*, 2008). The pattern of these metabolic abnormalities in patients on TARV resembles that of the metabolic syndrome, which is known to increase the risk of cardiovascular disease. The cardiovascular impact of these metabolic abnormalities has been poorly evaluated and data on their association with antiretroviral drugs have been inconsistent and contradictory (Barbaro *et al.*, 2003; Friis-Moller *et al.*, 2007 and Worm *et al.*, 2010). Preliminary studies indicate increased cardiovascular morbidity among HIV-infected individuals, suggesting that measures to reduce cardiovascular risk should be provided (Worm *et al.*, 2010; Depairon *et al.*, 2001; Torriani *et al.*, 2008 and Guimarães *et al.*, 2010), however, the implications of lipid disorders in this population are not yet fully known.

Dyslipidemia has emerged as an important problem affecting HIV-infected patients on ART as well as hypertriglyceridemia. The HIV Medical Association of the Infectious Disease Society of America and the Adult AIDS Clinical Trials Group Cardiovascular Subcommittee drew up guidelines (Dube *et al.*, 2003) for the evaluation and management of dyslipidemia based on a report published by the Adult Treatment Panel – ATP of the National Cholesterol Education Program – NCEP (NCEP III, 2001 and Grundy *et al.*, 2004). These recommendations included target lipid levels and treatment of dyslipidemia in patients with HIV infection, in accordance with the estimated global cardiovascular risk calculated using the Framingham risk function, with particular attention to potential drug interactions with antiretroviral agents (ARV) and maintenance of virological control of HIV infection (Dube *et al.*, 2003). All ATP reports have identified low-density lipoprotein cholesterol (LDL-c) as the primary target of cholesterol-lowering therapy and studies have shown that high serum concentrations of LDL-c are a major risk factor for coronary heart disease (CHD) (Shepherd *et al.*, 2002 and Ford *et al.*, 2002).

It is important to assume that dyslipidemia in HIV-infected patients, virologically well-controlled or not will have similar or even greater, long-term consequences than the general population will. Although unproven, the good results of lipid-lowering interventions will also be extending to HIV-infected individuals.

Despite the need of lipid-lowering drugs in some HIV-infected individuals, therapeutic lifestyle changes remain an essential modality in clinical management. In most instances, non pharmacological interventions should be first instituted and nutritional support should be considered in order to achieve the desired effects on lipid metabolism abnormalities. Therefore, the aim of this work was to evaluate the effects of dietary intervention on serum lipids, saturated fatty acids (SFA) and trans-fatty acids in HIV-infected individuals on ART.

Patients and methods

Design and subjects

This was a non-randomized, non-controlled nutrition intervention study in which HIV-infected adult patients were recruited from the outpatient clinic of a reference center for infectious and parasitic diseases (*Centro de Referência de Infecções Parasitárias Orestes Diniz* of the *Universidade Federal de Minas Gerais*, Brazil), between October 2005 and December 2006. Inclusion criteria were: HIV-positive individuals as confirmed by polymerase chain reaction; age ≥ 18 years old; patients who have been receiving ARV drugs at the same dose for a minimum period of 3 months prior to admission. Exclusion criteria

were: metabolic disorders such as hyperlipidemia and diabetes mellitus; presence of lipodystrophy prior to the diagnosis of HIV infection; use of glucocorticoids or any other steroids, growth hormone, beta-blockers, thiazide or any drugs associated with metabolic abnormalities and body fat redistribution; any relevant clinical event at the time of enrollment to the study; pregnancy or breastfeeding; abnormal liver function tests; abnormal renal function; abnormal thyroid function; reported or proven history of alcohol or drug abuse; psychiatric conditions; patients who had interrupted the use of ARV drugs; patients who had attended only the first nutritional counseling session; refusal of the patient to participate.

All selected patients received detailed information about all steps of the study and signed a written informed consent form. The study was approved by the ethics committee and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

During the routine medical evaluation in the referral center 469 HIV-infected individuals were recruited, according to the order of arrival. Only 98 patients fulfilled the inclusion criteria and signed the informed consent form. Forty-one patients were excluded because they had attended only the first nutritional counseling session (Figure 1).

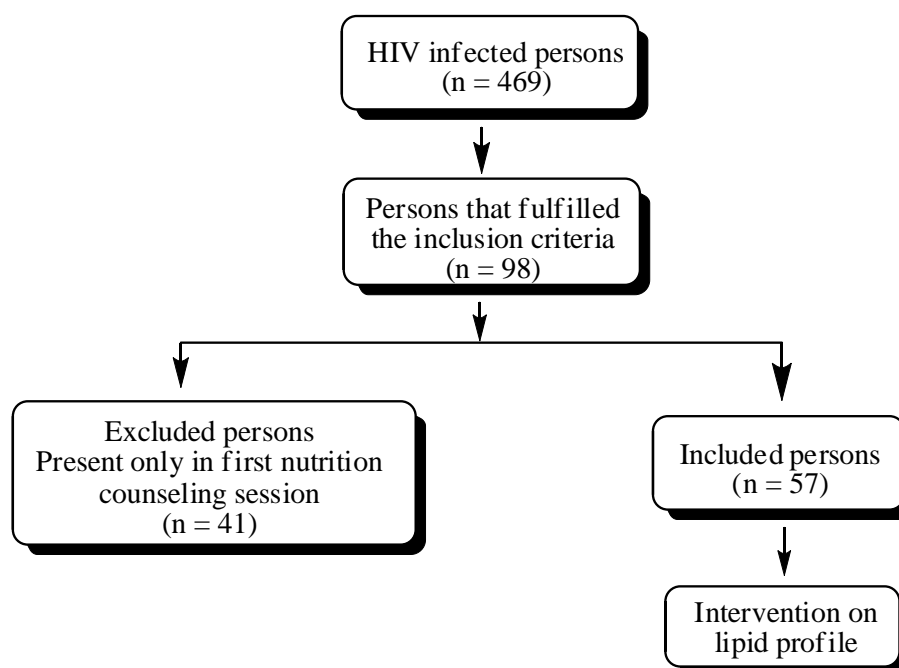


Figure 1: Selection scheme of the HIV patients on antiretroviral therapy (ART) that were submitted to nutritional counseling aiming an adequate lipid profile.

Clinical evaluation

All individuals included were evaluated following an ambulatory protocol. During the screening visit, blood tests were requested and the first appointment with a nutritionist was scheduled. Adherence to the study was secured through contact by telephone when it took the

confirmation of the date of appointment or reschedule. Data collected at first contact included age, gender, educational level, medical history, family history of chronic diseases, anthropometric measures and serum lipids levels from medical records. All participants completed a 24h recall. Information about the use of hypolipemiant and ARV drugs were also obtained from medical records.

The first nutritional counseling session was then conducted with the objective of reducing dietary intake of total lipids, saturated fatty acids and trans-fatty acids. The group received counseling by the nutritionist such as food groups and specific items, frequency, and portion size of each food group to be consumed, and they were asked to follow a specific daily food plan. The food plan included daily consumption of whole grains and products, 3 fruits, 2 portions of dark green vegetables, 2 portions of dark yellow vegetables and 2 units of Brazil nuts (10 grams). The participants were also instructed to reduce intake of red meat, replacing it by chicken or fish, to substitute margarine for halvarine or fruit jam or ricotta/yogurt pâté, to use olive oil for salad dressing, to use soy oil for cooking, to reduce/eliminate their intake of fried foods and sandwiched cookies, and increase the intake of low-fat milk. The same investigator gave all the information about the food plan. After the first nutritional counseling, another blood lipids tests were requested, to be carried out one week prior to the next visit.

During this study, the participants had at least two sessions of nutrition counseling and the 24-hour recall was completed using a photograph album of food portions (Zabotto, 1996) to help them to identify the size of portions. The quantity of food and/or preparations not illustrated in the photo album was estimated in accordance with the report given by the patient. The 24-hour recall was used to measure dietary intake, in both the beginning and at the end of the study, to verify the acceptability and compliance with the established methodology and to reinforce the key principles of the diet.

Laboratory measurements and dyslipidemia classification

Blood samples were taken after 12 h overnight fasting. The venous blood was collected with EDTA and plasma aliquots were obtained by ultracentrifugation. Total cholesterol (Tc) and triglycerides (Tg) were measured using the dry-chemical method in a Johnson chemical analyzer, model Vitros 750 or 950, with a Johnson (kit, Rochester, NY, USA. High-density lipoprotein cholesterol (HDL-c) was measured by immunoinhibition assay using a Roche Benchtop Analyzer, model Cobas Mira, and a Labtest (kit, Lagoa Santa, MG, Brazil. Serum Low-density lipoprotein cholesterol (LDL-c) was calculated from quantitative measurements of total cholesterol and HDL-cholesterol and plasma triglycerides

- Friedewald formula (Friedewald, 1992). Subjects were considered dyslipidemic according to the following recommended cutoff points: $Tc \geq 240$ mg/dl (hypercholesterolemia), Tg between 200 to 499 mg/dl (hypertriglyceridemia), and $Tg \geq 500$ mg/dl (very high hypertriglyceridemia) (NCEP III, 2001).

Energy and nutrient intake

The analysis of the 24-h recall was carried out with the use of DietWin diet analysis software (Reinstem, 1998).

Anthropometric Measurements

The anthropometric measurements were carried out by a single observer (the investigator). Data collected were weight (kg), height (cm), body circumferences (cm) and skinfold thickness (cm). Weight was measured using a mechanical platform scale (Welmy Indústria e Comércio de Balanças Ltda, São Paulo, SP, Brazil), with a maximum capacity of 150 kg and increments of 100 grams. Height was measured using a wooden stadiometer fixed to the wall of the consulting room. The measurements of body circumference (abdomen, hip and arm) were obtained using a 0.7 cm wide, non-elastic measuring tape (defined as the smallest measurement between the lateral iliac crest and the lowest rib) and hip circumference (measured at the level of the widest circumference over the greater trochanters) (Leite *et al.*, 2000). Skinfold thickness (tricipital, bicipital, supriliac and subscapular) measurements were taken using an adipometer (Lange Skinfold Caliper, Beta Technology Inc., Santa Cruz, CA, USA). The skinfold thickness measurements were taken in triplicate, always on the right side of the body and fat percentage was calculated, using both the caliper method (Durnin & Womersley, 1974).

Statistical analysis

The data entry was performed using the Epidata software program, version 3.1 (Lauritsen; 2005). All the statistical analyses were carried out using the Stata software program, version 9.0 (Stata, 2006), and significance level was established at 95%. Normality was evaluated with the Shapiro-Wilk test and we used the Wilcoxon test for two matching variables and Student's t-test for paired data were used to compare the biochemical, anthropometric and dietary data collected at the end of study with those collected at baseline for all subjects and for groups according to exposition to lipid-lowering drugs (Armitage, 1995).

Results

Clinical and biochemical data were collected from 57 HIV-infected patients, aged 28.4 to 68.4 years (44.9 ± 9.4 years), before and after nutritional counseling. The majority of patients were male (65%), with at least 8 years of schooling (52.5%). The mean body mass

index (BMI) was 24.04 kg/m² (16.2 to 35.2 kg/m²) and 38.5% had BMI \geq 25 kg/m². Forty-eight (84%) patients had a family history of chronic diseases and the most common were coronary events (50%). All patients were exposed to antiretroviral therapy and 51% were using ART with Protease Inhibitor (PI). Twelve patients (21%) had a very low HDL-c and 26 patients (45.5%) had hypertriglyceridemia (Table 1).

Table 1 - Demographic, clinical, biochemical and treatment data of HIV-infected patients (n=57)

Parameter	n	%
Gender		
Male	37	65.0
Female	20	35.0
Education level (years of study)		
0	4	7.0
<8	30	52.5
\geq 8	23	40.5
BMI (kg/m²)		
<18.5	5	9.0
18.5-24.99	30	52.5
\geq 25	22	38.5
Family history of chronic diseases		
No	9	16.0
Yes	48	84.0
Stroke (yes)	13	27.0
Coronary event (yes)	24	50.0
ART		
with IP	29	51.0
without IP	28	49.0
Serum lipids		
HDL-c very low	12	21.0
Hypertriglyceridemia	26	45.5
Very high hypertriglyceridemia	1	2.0
Hypercholesterolemia	8	14.0
Hypertriglyceridemia and hypercholesterolemia	4	7.0
Very high hypertriglyceridemia and hypercholesterolemia	6	10.5

BMI: body mass index / IP: Protease inhibitor / HDL-c: High-density lipoprotein cholesterol

The median time of diagnosis of HIV infection was 6.74 \pm 3.32 years and three of them (5.0%) were aged \geq 60 years. At the baseline and at the end of the study 14 (24.5%) and 12 (21%) subjects had detectable viral load (p=0.82), respectively. Comparing the excluded individuals with those included, the family history and prevalence of diabetes (p=0.01) and arterial hypertension (p=0.009) were higher in the latter group.

There was a significant increase in carbohydrate, protein, selenium, and calcium intake and a significant decrease in total lipid, saturated fatty acids (SFAs), trans fatty acids (trans FA), and cholesterol after dietary intervention (Table 2). No significant difference was

observed in energy, total fiber, polyunsaturated fatty acids (PUFAs) and monounsaturated fatty acids (MUFAs) after dietary intervention (Table 2).

Table 2 - Nutrient intakes of HIV-infected patients at baseline and after dietary intervention (n = 57)

Parameter	Baseline		p
	Mean±SD (Median)	End of study	
Energy (Kcal)	2380.9±777.8 (2198.0)	2481.8±992.5 (2179.4)	0.83
Carbohydrates (%)	50.1±9.4 (50.6)	54.1±5.8 (54.6)	0.02
Proteins (%)	15.8±2.8 (15.4)	16.8±2.4 (16.6)	0.04
Total Lipids (%)	33.7±8.6 (32.8)	29.1±5.3 (28.5)	0.002
SFA(%)	9.9±4.4 (9.8)	7.5±2.8 (6.8)	0.0004
Trans FA (g)	3.1±3.3 (2.0)	1.9±3.8 (0.0)	0.0005
PUFA (%)	7.4±3.0 (7.1)	7.1±3.2 (6.8)	0.53
MUFA (%)	10.1±4.1 (9.7)	10.2±5.1 (9.8)	0.46
Total cholesterol (mg)	249.1±158.7 (217.7)	171.1±98.0 (180.3)	0.0004
Total fiber (g)	41.2±16.5 (41.5)	45.6±19.7 (40.0)	0.20
Selenium (µg)	33.1±136.2 (0.0)	44.3±83.7 (13)	<
Calcium (mg)	683.9±571.9 (594.0)	986.5±486.6 (823.5)	0.0007

SFA: saturated fatty acid/Trans FA: trans fatty acid/PUFA: polyunsaturated fatty acid
MUFA: monounsaturated fatty acid

Fridman and Wilcoxon tests

There was statistically significant decrease in suprailiac skinfold, waist and hip circumferences, and in Tc, VLDL-c, LDL-c after dietary intervention (Table 3).

Table 3 - Anthropometric and serum lipids data of HIV-infected patients at the baseline and at the end of the study (n= 57)

Parameter	Baseline		p
	Mean±SD (Median)	End of the study	
BMI (kg/m ²)	24.0±3.8 (24.1)	24.0±3.4 (23.6)	0.09
Circumferences (cm)			
<i>Waist</i>	87.3±10.9 (87.5)	86.3±10.0 (86.5)	0.02
<i>Hip</i>	91.3±8.1 (90.0)	90.6±6.4 (89.5)	0.01
<i>Arm</i>	33.2 ±3.8 (28.0)	28.4±3.2 (29.0)	0.18
Skinfold thickness (mm)			
<i>Tricipital</i>	13.5±7.2 (12.0)	13.5±6.4 (12.0)	0.50
<i>Bicipital</i>	7.3±3.8 (6.0)	7.3±3.8 (6.0)	0.84
<i>Suprailiac</i>	20.8±13.8 (16.0)	20.1±12.8 (16.5)	0.005
<i>Subscapular</i>	27.5 ±13.0 (25.0)	28.4±12.2 (27.0)	0.81
Serum lipids (mg/dl)			
Tc	217.6±48.6 (218.0)	202.1±48.1 (201.0)	0.0007
VLDL-c	45.3±6.7 (46.0)	40.2±17.1 (38.5)	0.03
LDL-c	128.6±48.5 (131.0)	117.4±39.6 (112.0)	0.02
HDL-c	40.5±10.4 (39.5)	42.0±11.7 (40.0)	0.32
Tg	303.2±206.6 (238.0)	229.9±119.6 (210.0)	0.0001

Tc: Total cholesterol/VLDL-c: Very low-density lipoprotein cholesterol/LDL-c: Low-density lipoprotein cholesterol/HDL-c: High-density lipoprotein cholesterol/Tg: Triglycerides

Fridman and Wilcoxon tests

Discussion

Metabolic disorders have been described in HIV-infected individuals on ART and have become an important clinical challenge in the global management of the disease (Dube *et al.*, 2003). The nutritional aspects of HIV infection have changed over the last years and the weight gain, fat redistribution, obesity, and dyslipidemia, characterized by hypertriglyceridemia and/or hypercholesterolemia, are the new nutritional problems of those individuals (Shevitz, 2001).

In these three months of non-randomized trial was suggested that nutritional intervention based on the NCEP ATP III guidelines (NCEP III, 2001) was able to prevent dyslipidemia induced by ART in HIV-infected patients. The nutritional counseling resulted in significant decreased in the serum levels of total lipids, namely, Tc, VLDL-c, LDL-c, Tg and significant increase in intake of calcium and selenium (Tables 2 and 3). These results are consistent with previous uncontrolled and controlled studies. Barrios *et al.*, 2002 found a significant reduction in Tc and Tg in 230 HIV infected patients on antiretroviral therapy, who had good compliance to a low-fat diet for 6 months. The reduction in Tg levels was greater than in Tc levels. Batterham *et al.*, 2003 showed in a retrospective study that there were significant reductions in Tc and Tg after changes in the diet. Recently, Lazzaretti *et al.*, 2012 demonstrated in a randomized clinical trial with 83 HIV-infected patients that dietary intervention prevents dyslipidemia associated with ART. The authors showed that in the group that received dietary intervention, the mean plasma levels of Tc, Tg, LDL-c, and BMI remained stable during the 12-month follow-up, while the control group presented the expected increment.

HIV/AIDS has many faces as described by Mahlungulu *et al.* in 2009. There are major differences between HIV-positive individuals in developed and developing countries with regard to income level, availability of adequate nutrition, and access to basic healthcare or life-prolonging antiretroviral treatment. In addition, patient groups vary in terms of their response to the virus, stage of the disease, susceptibility to secondary infections, nutritional status, and individual response to the various treatments received. These complexities must be taken into account when formulating recommendations and guidelines on nutrient and energy for HIV-infected individuals. The nutritional guidelines used in this study focused on the quality of the lipids consumed, with the purpose of reducing the SFA and trans FA, and increasing MUFAs and PUFAs and fibers, as well as decreasing daily cholesterol intake. The decrease in intake of total lipids, SFA, trans FA, and cholesterol was the result of the recommendations for reducing the intake of red meat and replace it with chicken or fish,

substituting margarine for halvarine/fruit jam/ricotta or yogurt pate, use olive oil for salad dressing, using soybean oil for cooking, and reducing/eliminating their intake of fried foods and sandwich cookies, likewise, increasing the intake of low-fat dairy products (Table 2). These results are similar to those described by Lichtenstein *et al.*, 1997, in which showed that the intake of foods with low level of trans FA and SFA was associated with decreased serum cholesterol. These findings are also corroborated by other studies (Mahlungulu *et al.*, 2009; Fitch *et al.*, 2006; Harnack, 2009).

Adequate nutritional education promotes and maintains optimal immune function. Dietary support may, therefore, improve clinical outcomes in HIV-infected individuals by reducing the incidence of HIV-associated complications and attenuating the progression of HIV disease. Weight loss, muscle wasting and malnutrition are common in patients with HIV infection or AIDS (Vorster, 2004) and remain significant clinical problems (Grinspoon & Mulligan, 2003). Variation in the nutritional composition, as well as differences in the disease stage of the HIV-infected patients can significantly affect intake and absorption of food (Mahlungulu *et al.*, 2009). There is evidence of severe protein deficiency in HIV/AIDS patients (Amadi *et al.*, 2001; Kurpad *et al.*, 2004) and protein deficiency is closely associated with energy deficiency. In the absence of adequate energy intake, body fat and protein are used as fuel sources. Fat is usually lost first and as body fat stores become progressively depleted, protein depletion becomes more striking. These changes are widely described in many wasting illnesses, but HIV seems to induce a special metabolic effect in the host involving a preferential loss of protein over fat (Macallan *et al.*, 1995). Beside this, rates of protein turnover usually increase in HIV/AIDS (Macallan *et al.*, 1995, 1998 e 2001; Harrison *et al.*, 2002 and Yarasheski *et al.*, 1998).

Direct evidence for specific clinical benefit from known increments of protein intake is largely lacking and will depend on the nutritional and inflammatory state of the patient. The absence of carefully performed trials of nutritional supplementation makes it difficult to be absolutely certain as to how much nutrition intervention will improve the outcome of HIV/AIDS. However, it seems reasonable to assume that nutritional interventions in HIV/AIDS will enhance the defense of the organism against opportunistic infections, promote recovery and improve quality of life and survival despite the lack of properly conducted trials.

In the meantime the overall evidence suggests that protein intake should be increased by 10% to match the increased intake of energy that is needed in HIV infected people (Hommes *et al.*, 1991; Melchior *et al.*, 1993; Grunfeld *et al.*, 1992; Grinspoon *et al.*, 1999).

This should be continued to maintain body nutrient stores during the chronic asymptomatic phase of HIV. When immunity fails and an opportunistic infection occurs, encouragement should be given to the patient to keep going with the extra 10%. It is unlikely that they will be able to eat any more than this if they are feeling unwell. Once the opportunistic clinical infection has cleared, additional amounts of energy and protein up to 30 to 50% over the customary intake should be encouraged to achieve nutritional recovery. Through this study was observed a significant increase of protein intake after nutritional intervention (Table 2). Although this recommendation is not yet a consensus and further controlled studies are needed, it would be important to maintain the balance between anabolism and catabolism of proteins. Scarcella *et al.* (2011) conducted a retrospective cohort study with 106 HIV/AIDS adult patients (84 in ART), all receiving food supplementation and peer-to-peer nutritional education. Nutritional status improvement was observed in both groups: with and without ART. However, the improvement in BMI was significant and substantially higher in ART patients because of the impact of ART on nutritional status of AIDS patients. The authors concluded that there was a synergic effect of integrating food supplementation, nutritional education and ART on the nutritional status of African AIDS patients. This finding highlights the importance of nutritional education in those patients.

The patients also had an increase in calcium and selenium intake (Table 2). The observed increase in calcium intake was associated with the orientation of patients to enhance the intake of low-fat dairy products and dark green vegetables. The increase in selenium intake was correlated to the advice to consume two units Brazil-nut daily. This fact may have contributed to the observed changes in lipid profile of the patients, since it has been postulated that the antioxidant nutrient deficiency could be related to the development of hypercholesterolemia (Kang, Mehta and Bansal, 2000; Sabaté *et al.*, 1993 and Kris-Etherton *et al.*, 1999).

According to the results, the decrease of serum Tg, Tc, VLDL-c and LDL-c was due to the nutritional intervention and not caused by reduced energy intake or by reducing the individuals' weight (Table 2). Despite not having been observed change in body weight, there was a decrease in waist and hip circumferences and skinfold suprailiac, which suggest that changes in nutrients intake caused mobilization of adipose tissue in the central region of the body (Table 3).

It is well known that HIV patients on ART may present body changes such as accumulation (lipohypertrophy) and/or with loss (lipoatrophy) of body fat (Sprinz *et al.*, 2010) and previous cohort study in the ART have consistently found an increase in body

weight after the diagnosis of HIV (Crum-Cianflone *et al.*, 2010). The patients presented mean BMI within the limits of normality at baseline and at the end of the study (Table 3). After the dietary intervention some of the anthropometric changes associated with the lipodystrophic syndrome were probably prevented. Lipodystrophic syndrome is associated with accelerated lipolysis, which leads to futile cycling (Sekhar *et al.*, 2002). In addition, lipodystrophy contributes to insulin resistance, diabetes mellitus and changes in fat distribution, characterized by loss of peripheral deposits and/or accumulation of visceral adiposity (Guimarães *et al.*, 2007; Guimarães *et al.*, 2008 and Crum-Cianflone *et al.*, 2010). All these metabolic abnormalities can lead to increased risk of cardiovascular disease. Guimarães *et al.*, 2007 demonstrated a strong correlation between intra-abdominal fat thickness and independent risk factors of cardiovascular disease: atherogenic lipid profile and insulin resistance. The increased waist circumference can be the expression of at least two fat components, visceral and subcutaneous ones. In particular, the visceral adipose tissue compartment, site of the local production of adipokines, is not an inert fat depot but a 'metabolically active' one, with different impacts on cardiovascular risk factors and on atherosclerotic vascular damage (Carr & Cooper 2000; Nicklas *et al.* 2004; Kuk *et al.*, 2006; Ronti, Lupattelli & Mannarino, 2006; Després *et al.*, 2008 and Lupattelli *et al.*, 2011). Studies performed before the advent of ART associated HIV infection with low HDL-c levels (Grunfeld *et al.*, 1992). More advanced stages of HIV infection and lower CD4 lymphocyte count have been associated with lower HDL-c levels (Shor-Posner *et al.*, 1993) and it has been shown that HDL-c levels may remain low despite ART (Riddler *et al.*, 2003). However, Scarcella *et al.*, 2011 showed significant increment in HDL-c with ART. The data found in this work did not show increase in serum levels of HDL-c. It could be because this lipoprotein frequently increases with the level of physical activity. The patients were mostly sedentary and remained so throughout the study, although they had been instructed to walk daily (Table 3). However, this study was not designed to evaluate the role of physical exercise on lipid profile.

At present, there is no enough evidence that physical activity has considerable benefits for lipid control in HIV infected patients. Terry *et al.*, 2006 concluded that 30 HIV infected patients with lipodystrophy and dyslipidemia submitted to a short-term intervention of low-lipid diet and aerobic exercise training (12 weeks) were able to increase their functional capacity without any consistent changes in plasma lipid levels. Fitch *et al.*, 2006 also failed to show improvement in lipid profile in a randomized study with 28 HIV-infected individuals with metabolic syndrome whose were submitted to an intensive lifestyle

modification program, which included a dietary intervention and physical activity. After 6 months, despite improvement in anthropometric variables, blood pressure and physical activity, there were no consistent changes in lipid profile.

Limitations

Some limitations were noted and must be acknowledged in this study. Although it is a prospective study, the number of subjects was not high, thereby limiting the power and accuracy of the analysis. Indeed, this did not allow us to carry out the linear regression analysis in order to evaluate the effects of dietary components on serum lipids adjusting to the use of antiretroviral drugs, as well as the associations could not be said to be causal. Other limitation was the lack of HIV-negative controls. Despite limitations, these findings suggest a good effect of dietary intervention in preventing dyslipidemia in this setting.

Conclusion

ART is associated with potentially atherogenic adverse lipid profile in HIV infected patients and measures to reduce cardiovascular risk should be provided. Current guidelines recommend the diet as a first - step intervention for those individuals with ART-related dyslipidemia and nutritional support should be considered in order to achieve the desired effects on lipid metabolism abnormalities. By the results of this work was possible to suggest an efficacy of nutritional intervention in the prevention of changes in lipid profile of HIV-positive individuals on ART. These findings also indicate that nutritional intervention should be considered for all patients on ART. However, we do believe that prospective randomized controlled studies are the key to test the effectiveness of dietary intervention in revert marked changes in lipid profile in HIV patients on ART and to evaluate the impact of this intervention on clinical outcomes associated with lipid profile.

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