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Original/*Otros*

Relationship between dietary intake and use of protease inhibitors with anthropometric and biochemical parameters of lipodystrophy in people living with HIV

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Abstract

The lipodystrophy syndrome is characterized by redistribution of body fat and disorders of glicidic and lipid metabolism. Although its etiology is related to infection and drug therapy, there is little evidence regarding the nutritional disturbances on this association. This study aimed to assess the relationship between dietary intake and use of protease inhibitors (PIs) with anthropometric and biochemical parameters in HIV positive patients. The study included 50 patients. A questionnaire about socioeconomic status, lifestyle and infection history was taken. In addition, it was conducted the evaluation of dietary intake (frequency questionnaire), anthropometric parameters (body mass index, waist circumference, triceps skinfold, corrected arm muscle area) and biochemistry tests (glycemia and lipid profile). Only 37% of the sample was classified as "good food consumption", 54% were overweight or obese and 66% presented high waist circumference. The group with good food consumption had higher HDL-C (p=0.04) levels than the group with poor food consumption. Patients taking PIs presented VLDL-C (p=0.023) and triglycerides (p=0.024) levels significantly higher. These results indicated the necessity for continuous monitoring of HIV-positive patients and non-pharmacological interventions such as nutrition education and practice of physical exercises.

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Key words: *Diet; Lipodystrophy; HIV; High Active Antiretroviral Therapy*

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RELACIÓN ENTRE LA DIETA Y LA INGESTA Y EL USO DE INHIBIDORES DE LA PROTEASA CON PARAMÉTROS ANTROPOMÉTRICOS Y BIOQUÍMICOS DE LA LIPODISTROFIA EN LAS PERSONAS QUE VIVEN CON HIV

Resumen

La lipodistrofia se caracteriza por la redistribución de la grasa corporal y los trastornos de la glucosa y el metabolismo de los lípidos. Su etiología está relacionada con la infección y la terapia de drogas, sin embargo, hay poca evidencia sobre el papel de la nutrición en estos cambios . Este estudio tuvo como objetivo evaluar la relación entre el consumo alimenticio y el uso de inhibidores de la proteasa con parâmetros antropométricos y bioquímicos en las personas que viven con el VIH. La muestra estuvo constituida por 50 pacientes. Se recogieron Preguntas sobre la situación socioeconómica, el estilo de vida, y antecedentes de infección. Además, se celebró evaluar el consumo de alimentos (cuestionario de frecuencia), antropométricos (índice de masa corporal, circunferencia de la cintura, espesor del pliegue cutáneo del tríceps y el área muscular del brazo corregida) y bioquímicos (niveles de glucosa y lípidos). Sólo el 37 % de la muestra se clasifica como buena consumo de alimentos, 54 % tenían sobrepeso o eran obesos y 66 % tienen alta circunferencia de la cintura. El grupo de consumo de alimentos clasificados como " buenos" presentaram mejores valores de HDL-c cuando comparados com el grupo clasidicado del "malo" del los pacientes que usan IP mostró valores de VLDL -C y triglicéridos significativamente más altos. Estos resultados indican la necesidad de un seguimiento continuado de estos pacientes y las intervenciones no farmacológicas, como la educación en nutrición y ejercicio físico.

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Palabras clave: *Dieta, Lipodistrofia, HIV, La terapia antirretroviral altamente activa.*

Abbreviations

HAART: High Active Antiretroviral Therapy
PVHIV: Persons Living with HIV
IP: Protease inhibitor
GTH: Giselda Trigueiro Hospital
BMI: Body Mass Index
WC: Waist circumference
CAMA: Corrected arm muscle area
TSF: Tricipital Skinfold
TEM: Technical Error of Measurement
TG: Triglycerides
TC: Total Cholesterol
HDL-c: High-Density Lipoprotein Cholesterol
LDL-c: Low-Density Lipoprotein Cholesterol
VLDL-c: Very Low-Density Lipoprotein Cholesterol

Introduction

Highly active antiretroviral therapy (HAART) has provided increased survival and quality of life of people living with HIV (PLHIV).[1] Despite these benefits, this therapy can lead to important metabolic changes, disturbances in glicidic and lipid metabolism, such as glucose intolerance and dyslipidemia. Furthermore, there is a redistribution of body fat, with loss of peripheral adipose tissue and central fat accumulation. It characterize the lipodystrophy syndrome, which increases the risk of cardiovascular diseases.[2]

The etiology of lipodystrophy is related with the infection itself, as with the use of antiretroviral therapy, especially protease inhibitors (PIs). The susceptibility of PLHIV to metabolic changes varies and it is influenced by several factors, such as time of infection, therapy, genetics and lifestyle (dietary intake and practice of physical exercises)[3].

Whereas the diet is related to occurrence of metabolic complications in PLHIV and nutritional assistance it has been valued this recognition to this group of patients. However, there is a lack of accurate information about possible associations between dietary profile and clinical-nutritional status using HAART[4]. Based on that, this study aims to assess the relationship between dietary intake and use of PIs with anthropometric and biochemical parameters in PLHIV.

Methods

This is a descriptive and cross-sectional study conducted from February to June of 2013 at the Hospital Giselda Trigueiro (HGT), which the service is reference of Infectious Diseases treatment in Rio Grande do Norte, Brazil. The convenience sample consisted of 50 patients (26 male and 24 female) with HIV that were in HGT to perform routine biochemical exams. After blood collection, the patients who fit the criteria were approached and invited to participate in the study. The Research Ethics Committee of the Federal University of Rio Grande do Norte approved the study (Protocol 229/11) and all participants signed and informed consent form.

The inclusion criteria consisted in age over 18 years, using antiretroviral therapy for at least 2 months and have medical request of all biochemical parameters requested for the study. The exclusion criteria consisted in drugs abuse, pregnancy, mental illness and those with any acute or chronic condition that had an impediment to respond the questionnaires or the anthropometric assessment.

The data were collected in a reserved room, respecting the privacy and the confidentiality. Were performed anamnesis, anthropometric assessment, dietary intake and biochemical profile of the participants.

The anamnesis was constituted by the identification of the patients (name and date of birth) and 23 questions subdivided into four categories: socio-economic aspects (income, education, marital status, occupation, and housing), family history of disease, lifestyle (alcohol consumption, smoking and regular practice of physical activity) and infection history (transmission, time of diagnosis, time and type of HAART, HIV family history). The information regarding the infection history were confirmed in the medical records of the subjects.

The anthropometric parameters were Body Mass Index (BMI), Waist Circumference (WC), Corrected Arm Muscle Area (CAMA) and Triceps Skinfold (TSF). The body mass, height and other measurements were measured according to the protocol of the *International Society for the Advancement of Kinanthropometry* (ISAK)[5]. The tools used in the evaluation were: Techline® digital scale with 100g precision and scale of 180 kg; Sanny® stadiometer with 2.10mm capacity and precision of 0.1 cm; Sanny® anthropometric tape and Harpenden® adipometer with 0.2mm scale and interpolation of measurement of 0.1 mm. The same researcher, which presents technical error of measurement (TEM) of 1.9% for triceps skinfold and 1.5% for circumferences, took all measures. The classification of BMI was based on the classification proposed by the WHO (1997)[6] for adults and Lipschitz (1994)[7] for the elderly subjects; waist circumference followed the WHO (2000)[8] recommendations.

The protocol for the dietary intake assessment was determined after conducting a pilot study. Due to the educational level of the subjects, it was found a low level of understanding of a complex questionnaire[9]. In order to maintain the reliability of the data, the dietary intake was assessed qualitatively through a food frequency questionnaire from the Food and Nutrition Surveillance System (SISVAN) of the Brazilian Ministry of Health[10]. It asses the intake frequency of 10 food groups during the last seven days. Despite being a reduced questionnaire, it can represent specific groups of foods, which represent sources of specific nutrients such as fibers, saturated fat and simple carbohydrates.

The food intake analysis was adapted based of the study of Fornes (2002)[11], using the following equation: [Score = [1/7x frequency of consumption]. The classification was made by splitting the data in terciles.

Biochemical analysis was performed at the HGT Clinical Analysis Laboratory and the patients fasted for 12 hours. Was realized the blood collect on peripheral vein of 20 ml, which was centrifuged to 3000G during five minutes for to obtain serum, stored to -80° Celsius for later realization of dosages. Were dosed fasting glycemia, total cholesterol, LDL-c, HDL-c, VLDL-c and triglycerides by Trinder's method; for the TCD4+ lymphocytes count was used the technique of flow cytometry with the multi-test method; for the quantification of HIV-1 viral RNA (viral load) was used the bDNA method. The data of TCD4+ lymphocytes counts and viral load were obtained in the medical records, being registered the most recent information.

The statistical treatment followed the criteria of scientific authenticity. It was conducted according to the following order: distribution of data in a Gaussian curve of normality, through the non-parametric test of Shapiro-Wilk. Observing a wide variance in the distributions, it was opted to stratify the groups according to food consumption in terciles. The distribution analysis was repeated after the classification of lower third as "poor", middle third as "regular" and the upper third as "good". There was a rating about "use or not" of Protease Inhibitor, such strategy was given by its interference of this class of drugs in the lipid profile[12]. The inferences were made by comparisons such as hypothesis testing, considering an alpha value less than 5% or p-value < 0.05. The acceptance or rejection of the hypothesis indicated a probability of 95% of not making type I error. Accordingly, it was used the *One-Way* Anova with Scheffe post hoc test as hypothesis test in comparisons between parametric variables classified by groups of food intake. For the non-parametric variables, it was used the Kruskal-Wallis test, since the samples showed different sizes. Regarding the inference between groups of use or non-use of the inhibitor, it was used the *One-Way* Anova and the Mann-Whitney U-test to parametric and non-parametric variables

Results

The mean age of the total sample was 47.7 ± 11.5 years. There was a predominance of single adults (64%); in relation to the educational level, 4% were unlettered, 38% did elementary school, 40% completed the high school and 18% had higher education. In relation to lifestyle, 20% were smokers and 34% consume alcoholic beverages. The horizontal route transmission of the virus was reported in 68% of cases. The mean time from diagnosis and initiation of therapy was 8 years and 50% of the subjects made use of PIs in combination to the anti-retroviral treatment.

In relation to food intake, 37% of the sample was classified with "good" food consumption, 28% with "regular" food consumption and 35% as "poor" food consumption. Regarding practice of physical activity, 60% were inactive.

Table I
Biochemical and anthropometric variables according to the food consumption

Variables	*Food consumption Classification*			*Hypothesis test*		
	Mean (SD)			*p < 0.05*		
	Poor	*Regular*	*Good*	*Poor vs. Regular*	*Poor vs. Good*	*Regular vs. Good*
Blood glucose (mg/dL)	90.6 (8.16)	99.8 (12.77)	96.0 (14.90)	0.206	0.471	0.740
TG (mg/dL)	176.5 (63-669)*	121.0 (24-595)*	142.5 (53-307)*	0.132	0.233	0.500
TC (mg/dL)	208.6 (45.67)	209.5 (59.42)	216.9 (41.52)	0.999	0.889	0.920
HDL-c (mg/dL)	36.9 (8.77)	43.9 (12.15)	48.3 (14.89)	0.368	0.040	0.654
LDL-c (mg/dL)	120.0 (47.27)	127.6 (60.96)	124.2 (42.12)	0.945	0.983	0.983
VLDL-c (mg/dL)	35.3 (9-133)*	47.1 (31.13)	29.6 (11-251)*	0.784	0.726	0.410
Body mass (Kg)	69.3 (13.14)	63.7 (12.24)	72.2 (14.28)	0.515	0.806	0.209
BMI (Kg/m^2)	25.8 (4.58)	26.7 (4.82)	24.8 (18.8-39.5)*	0.552	0.728	0.447
WC (cm)	91.9 (10.73)	88.2 (11.79)	91.9 (12.55)	0.683	1.000	0.674
TSF (mm)	10.0 (4.2-34)	13.9 (7.48)	11.6 (6.42)	0.777	0.708	0.382
CAMA (cm^2)	27.6 (3.49)	28.8 (3.67)	28.2 (4.46)	0.720	0.913	0.912

TG (mg/dL): Tryglicerides; TC (mg/dL): Total cholesterol; BMI (Kg/m^2): Body Mass Index; WC (cm): Waist circumference; TSF (mm): Triceps skinfold; CAMA (cm^2): Corrected Arm Muscle Area *Median (Variation).

Considering the whole sample, the mean BMI was 26.0 ± 4.7 kg/m^2, 34% were overweight and 20% of obese. In relation to the waist circumference, 66% were above the cut-off point considered at risk for development of metabolic abnormalities. The biochemical parameters showed an mean blood glycemia of 92.1 ± 12.6 mg/dL, 201.6 ± 46.4 of total cholesterol and 123.6 ± 47.4 mg/dL of LDL. The median of triglycerides was 148 mg/dL and VLDL 41 mg/dL.

In Table 1 it is shown the biochemical and anthropometric variables when the sample was divided according to food intake classification. Table 2 shows the sample divided according to the use of PIs in antiretroviral therapy combination.

In our study observed which group with food consumption "good" showed high levels of HDL in comparison to group with food consumption "poor", and the group using IP showed high levels of triglycerides and VLDL. The results showed the importance of the adequate diet ingestion how a protection factor, as well as IP utilization how a risk factor to development of cardiovascular diseases. However, there a few studies, specially in low socioeconomic status regions and in Brazil's Northeast, about the relation of lipodystrophy and the diet characteristics and the medicine treatment in PVHIV.

In relation to dietary intake, it was found that only 37% of the subjects interviewed presented food consumption classified as "good". The greatest inadequacies were represented by groups of vegetables and dairy products. In other studies, it was also observed that the patient's diet was not adjusted to their needs. Leite and/& Sampaio (2011)[14] identified inadequacy in the consumption of fish, vegetables and sugar; Duran (2008)[15] identified only 23% adequacy of the diet, with mismatches in the consumption of fruits and vegetables when evaluating the PLHIV consumption by food frequency questionnaires.

These results are concerning since the supply of energy and nutrients, as well as an adequate nutritional status are essential in the prognosis of patients with AIDS, including the immune response to opportunistic infections[16]. In addition, an unbalanced diet increases the risk for developing cardiovascular disease in HIV patients[17]. Accordingly, the World Health Organization recommends that nutritional interventions should be part of all programs of control and treatment of AIDS, it would contribute to a better adhesion and effectiveness of antiretroviral therapy[18].

Regarding anthropometric parameters, there was no significant difference in the classification of food consumption, as well as in the studies of Arendt (2008)[19], Duran (2008)[15] and Samaras (2009)[20]. This may be related with small sample, the limitation of the questionnaire used, with the reduced period of time this evaluates, or even influence the infection and HAART exerts on body composition in these patients. In addition, most of the patients studied were overweight, corroborating with Sahah (2005)[21] and opposed to the results of research conducted by Guimarães (2007)[22], Jaime (2004)[23], Ogalha (2011)[24], Cahan (2009)[25], in which this population presented appropriate weight (eutrophy). Concerning the accumulation of fat in the abdominal area, typical of lipodystrophy, was noted greater inadequacy in this parameter compared to the BMI. This fact has also

Table II
Biochemical and anthropometric variables according to the use of Protease Inhibitor

Variables	*Use of Protease Inhibitor*		*Hypothesis test*
	Yes	*No*	*p<0.05*
Blood glucose	93.9 (14.28)	96.3 (10.74)	0.556
TG	164.0 (33-669)*	114.0 (24-595)*	0.024
TC	204.3 (46.34)	221.6 (48.31)	0.246
HDL-c	39.5 (22-72)	46.4 (13.71)	0.154
LDL-c	116.7 (43.95)	130.6 (53.10)	0.441
VLDL-c	45.6 (9-251)*	26.7 (10.8-119.9)*	0.023
Body Mass	71.0 (14.90)	67.5 (11.75)	0.368
BMI	26.6 (5.56)	25.6 (3.88)	0.479
WC	92.2 (13.56)	89.8 (9.87)	0.504
TSF	14.3 (7.82)	8.0 (3.8-31.2)*	0.075
CAMA	28.3 (4.44)	28.4 (3.41)	0.945

TG (mg/dL): Tryglicerides; TC (mg/dL): Total cholesterol; BMI (Kg/m^2): Body Mass Index; WC (cm): Waist circumference; TSF (mm): Triceps skinfold; CAMA (cm^2): Corrected Arm Muscle Area *Median (Variation).

been reported in the study of Jaime (2004)[23]. Waist circumference values found in this study varied in the range described in the literature: 84.9 to 95.5 cm[22].

The group classified as "good" food consumption showed better levels of HDL-c, emphasizing the adoption of healthy diet practices could contribute to significatives changes, mainly in abdominal fat reduction and lipid profile in PVHIV (25-27). Was also observed which 76% of patients showed at least one parameter of lipid profile altered, being the LDL-c, the parameter with the major alterations in relation to references values.

The sample was divided according to the use of PIs in antiretroviral combination and there has been an increase of triglycerides and VLDL. According to studies, the use of PIs cause apoptosis of subcutaneous adipocytes and contributes to increased expression and secretion of Pro-Inflammatory Cytokines involved in Adipocyte function modification and reduction of adiponectin[29,30]. In addition, studies show that adipose tissue of patients receiving PIs presents a reduction in the expression of transcription factors involved in adipogenesis[31,32].

Corroborating with the results of this study, some researches proved the association between hypercholesterolemia and/or hypertriglyceridemia and use of PIs. Tsiodras et al. (2000)[33] observed cumulative incidence of approximately 20% of new cases of hypercholesterolemia and hypertriglyceridemia in patients with AIDS in PIs therapy during 5 years. Purnell et al (2000)[34] found high serum levels of total cholesterol, triglycerides, lipoproteins and lipoprotein B in the subject after studying healthy individuals infected with HIV not receiving PIs during 2 weeks. The increase in triglycerides in patients on use of PIs was also verified in another study of Tsiodras (2009)[26].

In relation to biochemical parameters, it was verified that a good diet was associated with better values of HDL-c, corroborating with the idea that healthy eating practices can contribute to significant changes, especially in the reduction of abdominal fat and lipid profile in PLHIV[26,27,28]. It was also noted that 76% of the patients had at least one lipid profile parameter change, with the LDL-c showing the greatest change in relation to the reference values.

With the Acquired Immunodeficiency Syndrome assuming the profile of chronic disease, non-pharmacological interventions have been recommended for the treatment of lipodystrophy syndrome in PLHIV[35]. In this way, studies like this should be developed in order to enlighten the relationship between food consumption and anti-retroviral therapy with parameters in lipodystrophy, contributing to the planning of safe and effective strategies for treating PLHIV.

The results of this study indicate the necessity for a continuous monitoring of patients of HIV-positive patients, especially those using PIs. Due to metabolic disorders caused by infection and the antiretroviral therapy the need for non-pharmacological interventions is are essential.

Conclusion

The group with food consumption classified as "good" obtained betters levels of HDL-c than the "poor" group. It was also observed that patients using PIs had significantly higher levels of VLDL-C and TG. These results indicate which adequate diet habits represent a protective factor, as well as IP use, a risk factor to development to cardiovascular diseases.

Conflict of interest

The authors declare no conflicts of interest.

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References

1. Marins JR, Jamal LF, Chen SY, et al. Dramatic improvement in survival among adult Brazilian AIDS patients. *AIDS* 2003;17:1675-1682.
2. Aboud M, Elgalib A, Pomeroy L, et al. Cardiovascular risk evaluation and antiretroviral therapy effects in an HIV cohort: implications for clinical management: the CREATE 1 study. *Int J Clin Pract* 2010;64:1252-1259.
3. Chen D, Misra A, Garg A. Lipodystrophy in human immunodeficiency virus-infected patients. *Journal of Clinical Endocrinology and Metabolism* 2002;87:4845-4856.
4. Kamerman Burns LA. ADA releases new position statement on nutrition and HIV. *HIV Clin* 2010;22:11.
5. Marfell-Jones TOM, Stewart A, Carter L. International standards for anthropometric assessment. Potchefstroom, South Africa: International Society for the Advancement of Kinanthropometry, 2006.
6. WHO – WORLD HEALTH ORGANIZATION – Preventing and managing the global epidemic of obesity. Report of the World Health Organization Consultation of Obesity. Geneva, 1997.
7. Lipschitz DA. Screening for nutritional status in the elderly. *Prim Care* 1994;21:55-67.
8. WHO. Obesity: Preventing and managing the global epidemic. Report of a consultation (2000). *WHO Technical Report, Series 894*. Geneva: WHO, 2000.
9. Ribeiro AC, Sávio KEO, Rodrigues MLCF, Costa THM, Schmitz BAS. Validação de um questionário de frequência de consumo alimentar para população adulta. *Rev Nutr* 2006,19:553-562.
10. Brasil, Ministério da Saúde. Formulário de marcadores do consumo alimentar para indivíduos com 5 anos de idade ou mais. Brasília: Ministério da Saúde. Available at http://189.28.128.100/nutricao/docs/geral/marcador_consumo_maiores_ 5_anos.pdf. Section accessed Jun 15, 2012.
11. Fornes NS, Martins IS, Velasquez-Melendez G, Latorre MRDO.

Escores de consumo alimentar e níveis lipêmicos em população de São Paulo, Brasil. *Rev. Saúde Pública* 2002;36:12-18.
12. Wanke C, Gerrior J, Hendricks K, McNamara J, Schaefer E. Alterations in lipid profiles in HIV-infected patients treated with protease inhibitor therapy are not influenced by diet. *Nutr Clin Pract* 2005;20:668-673.
13. Brasil, Ministério da Saúde. Boletim Epidemiológico AIDS e DST - 2012. Brasília: Ministério da Saúde, Departamento de DST, AIDS e hepatites virais. Available at http://www.aids.gov.br/publicacao/2012/boletim-epidemiologico-aids-e-dst-2012. Section accessed Feb 26, 2013.
14. Leite LH, Sampaio AB. Dietary calcium, dairy food intake and metabolic abnormalities in HIV-infected individuals. *J Hum Nutr Diet* 2010;23:535-543.
15. Duran AC, Almeida LB, Segurado AA, Jaime PC. Diet quality of persons living with HIV/AIDS on highly active antiretroviral therapy. *J Hum Nutr Diet* 2008;21:346-350.
16. Joint United Nations Programme on HIV/AIDS, World Health Organization, World Food Programme, 2008. HIV, food security and nutrition (expanded version). Available at http://www.hivpolicy.org/Library/HPP001507.pdf. Section accessed Jul 23, 2013.
17. Salyer J, Lyon DE, Settle J, Elswick RK, Rackley D. Coronary heart disease risks and lifestyle behaviors in persons with HIV infection. *J Assoc Nurses AIDS Care* 2006;17:3-17.
18. WHO - World Health Organization. Reports of a technical consultation. Nutrient requeriments for people living with HIV/AIDS. Geneva: WHO; 2003.
19. Arendt BM, Aghdassi E, Mohammed SS, et al. Dietary intake and physical activity in a Canadian population sample of male patients with HIV infection and metabolic abnormalities. *Curr HIV Res* 2008;6:82-90.
20. Samaras K, Wand H, Law M, Emery S, Cooper DA, Carr A. Dietary intake in HIV-infected men with lipodystrophy: relationships with body composition, visceral fat, lipid, glucose and adipokine metabolism. *Curr HIV Res* 2009;7:454-61.
21. Sahah 2005
22. Guimarães MM, Greco DB, Júnior ARO, Penido MG, Machado LJC. Distribuição da gordura corporal e perfis lipídico e glicêmico de pacientes infectados pelo HIV. *Arq Bras Endocrinol Metab* 2007;51:42-51.
23. Jaime PC, Florindo AA, Latorre MRDO, Brasil BG, Santos ECM, Segurado AAC. Prevalência de sobrepeso e obesidade abdominal em indivíduos portadores de HIV/AIDS, em uso de terapia anti-retroviral de alta potência. *Rev bras epidemiol* 2004;7:65-72.
24. Ogalha C, Luz E, Sampaio E, et al. A randomized, clinical trial to evaluate the impact of regular physical activity on the quality of life, body morphology and metabolic parameters of patients with AIDS in Salvador, Brazil. *J Acquir Immune Defic Syndr* 2011;57:179-185.
25. Cahn P, Leite O, Rosales A, et al. Metabolic profile and cardiovascular risk factors among Latin American HIV-infected patients receiving HAART. *Braz J Infect Dis* 2010;14:158-166.
26. Tsiodras S, Poulia KA, Yannakoulia M, et al. Adherence to Mediterranean diet is favorably associated with metabolic parameters in HIV-positive patients with the highly active antiretroviral therapy-induced metabolic syndrome and lipodystrophy. *Metabolism* 2009;58:854-859.
27. Lazzaretti RK, Kuhmmer R, Sprinz E, Polanczyk CA, Ribeiro JP. Dietary intervention prevents dyslipidemia associated with highly active antiretroviral therapy in human immunodeficiency virus type 1-infected individuals: a randomized trial. *J Am Coll Cardiol* 2012;59:979-88.
28. Hendricks KM, Dong KR, Tang AM, et al. High-fiber diet in HIV-positive men is associated with lower risk of developing fat deposition. *Am J Clin Nutr* 2003;78:790-795.
29. Domingo P, Malia-Guiu X, Pujol RM, et al. Subcutaneous adipocyte apoptosis in HIV-1 protease inhibitor-associated lipodystrophy. *AIDS* 1999;13:2261-2267.
30. Lagathu C, Kim M, Maachi M, et al. HIV antiretroviral treatment alters adipokine expression and insulin sensitivity of adipose tissue in vitro and in vivo. *Biochimie* 2005;87:65-71.
31. Bastard JP, Caron M, Vidal H, et al. Association between altered expression of adipogenese factor SREBP1c in lipoatrophic adipose tissue from HIV-1-infected patients and abnormal adipocyte differentiation and insulin resistance. *Lancet* 2002;359:1026-1031.
32. Shimomura I, Hammer RE, Richardson JH, et al. Insulin resistance and diabetes mellitus in transgenic mice expressing nuclear SREBP1c in adipose tissue: Model for congenital generalized lipodystrophy. *Genes Dev* 1998;12:3182-3194.
33. Tsiodras S, Mantzoros C, Hammer S, Samore M. Effects of protease inhibitors on hyperglycemia, hiperlipidemia ande lipodystrophy- a 5 years cohort study. *Arch Int Med* 2000;160:2050-2056.
34. Purnell J, Zambon A, Knopp R, et al. Effect of ritonavir on lipids and post-heparin lipase activities in normal subjects. *AIDS* 2000;14:51-7.
35. Brasil, Ministério da Saúde. Síndrome Lipodistrófica em HIV – Cartilha para profissionais da saúde. Brasília 2011: Ministério da Saúde, Departamento de DST, AIDS e hepatites virais. Available at http://www.aids.gov.br/sites/default/files/anexos/ publicacao/2011/50427/ vers_o_final_63134.pdf. Section accessed Feb 26, 2013.