

LEVELS OF PHYSICAL ACTIVITY AND METABOLIC ALTERATIONS IN PEOPLE LIVING WITH HIV /AIDS



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ABSTRACT

The introduction of Highly Active Antiretroviral Therapy (HAART) has deeply changed the course of HIV infection with increase in survival and improvement in quality of life as well as partial restoration of the immune system. After about ten years from the HAART use, the effects of combination treatment / virus started to come out. Among these, we can mention changes in lipid metabolism with hypertriglyceridemia, hypercholesterolemia, insulin resistance, hyperglycemia and redistribution of body fat as risk factors for cardiovascular disease. Observational studies with people living with HIV / AIDS evidence that when an individual finds out that he/she is an HIV/AIDS patient, he/she ends up feeling fear or shame, reducing hence social circle, work and leisure activities, and becomes isolated at home or in small groups which have common identity of HIV / AIDS patients. The purpose of this work was to evaluate the relationship between the level of habitual physical activity and recreation of people living with HIV / AIDS and its relation with metabolic changes. The patients were classified into active and sedentary, using the Habitual Physical Activity questionnaire proposed by Baecke and validated for HIV / AIDS patients. Classification was conducted according to the recommendations of the American College of Sports Medicine. Metabolism was assessed through plasma levels of glucose, total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides, using commercial kits. The sample consisted of 65 HIV patients who used HAART for at least five years. 64.6% were classified as sedentary and 35.4% as active. The study shows a direct relationship between physical activity level and higher levels of HDL - cholesterol in HIV / AIDS. HDL - Cholesterol is a lipoprotein of cardiovascular protection and, although other assessed parameters have not shown difference, these results highlight the need for additional studies on risk factors and physical activity for HIV / AIDS enabling proposals for specific interventions for these patients.

Keywords: HIV/AIDS, physical activity, metabolism.

INTRODUCTION

There are about 33.2 million people with the HIV virus worldwide, and in 2007 AIDS caused approximately 2.1 million deaths. In Brazil, between 1980 and June 2008, 506,499 cases of AIDS have been reported, with 205,409 declared deaths in the Mortality Information System (SIM). In Paraná, since the beginning of the epidemic, 23,144 cases of AIDS have been reported and the incidence of new recorded cases in 2006 alone was of 1,551¹.

In the beginning of the epidemic by the HIV virus, life expectancy of the infected subjects was extremely low. From the 90's, with the introduction of the highly active antiretroviral therapy (HAART) the disease history suffered serious alterations; increase in survival and improvement of quality of life, besides partial restoration of the immune system. However, after about 10 years of the HAART use, effects of the treatment/virus combination begin to appear on the body. These effects include alterations in the metabolism of lipids leading to hypertriglyceridemia, hypercholesterolemia and other metabolic alterations such as insulin resistance, hyperglycemia and body fat redistribution which are risk factors to cardiovascular disease². The combination of these alterations is known as HIV lipodystrophy syndrome (HIVLS). HIVLS, officially described by the

Food and Drug Administration (FDA) in 1997, is also known as syndrome of body fat redistribution, metabolic syndrome associated with the antiretroviral therapy (ARV) or, more recently, dyslipidemic lipodystrophy associated with HIV/HAART (HADL)³.

The lipid alterations found include low seric levels of HDL-cholesterol, increase of total cholesterol, LDL-cholesterol and triglycerides, which contributes to the onset of atheromatous plaques⁴. Additionally, the literature presents data which show probability of 100% of the cases in developing lipodystrophy – characterized by peripheral fat redistribution to the central region, especially abdominal – after 10 years of use of the antiretroviral therapy⁵.

Patients infected with the HIV even without use of the antiretroviral therapy present alteration in the lipid metabolism. Patients who have not initiated the antiretroviral therapy frequently present hypercholesterolemia with high LDL-cholesterol and low HDL-cholesterol, preceding hypertriglyceridemia⁶.

Patients who use the antiretroviral therapy present more frequent and severe hyperlipidemia. Some studies demonstrate incidence of 60% for hypercholesterolemia and 75% for hypertriglyceridemia, both more frequent in patients who use ritonavir, ritonavir-saquinavir and ritonavir-lopinavir⁷. The mechanisms which

lead to these alterations are not totally elucidated yet.

Endothelial dysfunction is another consequence of the metabolic alterations which may bring deleterious effects to the heart. It has been identified as a contribution to the onset and clinical manifestation of atherosclerosis when associated with dyslipidemia and type 2 diabetes⁸. However, not the endothelial dysfunction alone is related to atherosclerotic disease. A study by Cotter⁹ demonstrated that the plasma level of lipoprotein (a) is increased in 48% in the patients infected with HIV who make use of protease inhibitors. The meaning of these findings may be associated with premature atherosclerosis, regardless of the cholesterol level.

The introduction of the HAART in 1996 caused increase in mortality by coronary arterial disease, a fact related to the dyslipidemia and body fat redistribution verified in seropositive patients. A study – *The Data Collection on Adverse Events of Anti-HIV Drugs (DAD) Study Group* – published in 2003, which followed 23,468 HIV positive patients, showed increase in the incidence of acute myocardial infarct (AMI) with longer exposure time to the antiretroviral drugs³.

The handling of the dyslipidemia in the patient infected with HIV is crucial due to its potential atherosclerotic effect. According to the National Cholesterol Education Program Adult Treatment Panel III Guidelines (NCEP ATP III), the first step is to determine the risk factors which interfere in the LDL-cholesterol rates such as smoking, high blood pressure (> 140mmHg or use of anti-hypertensive drug), low HDL-cholesterol (< 40mg/dL), age (male sex > 45 years and female sex > 55 years) and family history of premature coronary disease (male first degree family aged < 55 years and female < 65 years).

Genetic predisposition¹⁰, inadequate diet¹¹ and physical inactivity¹² are among the main factors which contribute to the onset of metabolic alterations.

Physical activity is defined as any body movement caused by activation of skeletal muscles with increase in the energetic demand and consequent increase of metabolism. On the other hand, physical exercise is defined as planned, structured and repetitive physical activity. Both physical activity and exercise are related to good physical conditioning, improvement in the routine activities, better vigor and decrease of fatigue providing extra energy to the development of normal activities and in unexpected situations followed by stress¹⁷.

Sedentarism may be defined as lack of sufficient physical activity and is not connected to lack of sports practice. Individuals with regular physical activities such as housework, walking to work, performing professional tasks which require physical effort, are not classified as sedentary. It occurs when the subject presents low daily calorie expenditure with physical activities.

Observational studies in groups with people living with HIV/AIDS evidence that when the individual finds out he/she has the disease, a feeling of fear or shame is observed. The social circle, work and leisure activities decrease, contributing to isolation or restricted relations in small groups which present identify with the HIV/AIDS patient¹³.

Therefore, the aim of this work was to assess the relation between the level of activities of daily living and leisure activities of individuals living with HIV/AIDS and their relation with metabolic alterations.

METHODS

The studied population consisted of HIV/AIDS patients seen at the 15th Health Regional Unit-Maringá and 17th Health Regional Unit-Londrina, comprising 50 cities of the northwest region of Paraná. The sample was of patients who had minimum of five years of infection and used antiretroviral therapy (HAART). The patients were selected for the research after having received explanation about it in the STD/AIDS Units (Maringá and Londrina) where they signed the consent form approved by the Ethics in Research with Humans Committee of the State University of Maringá.

Socioeconomic data were collected using a closed questionnaire including: age, time of infection, family income, education, use of alcohol/illicit drugs, use of antiretroviral drugs, rate of TCD4+ lymphocytes and onset of opportunist infections.

The patients were later evaluated concerning their habitual physical activity through the application of the Baecke questionnaire for HIV/AIDS patients¹⁴. The instrument presents occupational physical activity (OPA), leisure physical activity (LPA), leisure and locomotion activities (LLA) and total (TS) scores. This instrument separated the patients in two groups: sedentary group (S) and active group (A). The guidelines of the American College of Sports Medicine were used for the classification.

Further information concerning leisure was obtained through a semi-structured interview approaching leisure habits before and after the HIV infection.

Each instrument was applied by the same evaluator, which guaranteed uniformity in the data contact as well as collection. The interviews were individual, previously scheduled in a set place and had average duration of 20 minutes. The analyses were performed according to the standardization and validation of each instrument.

Subsequently, the physical examination of the patients was performed with determination of fat percentage by bioimpedance using an HBF 306 INT Omron fat control monitor and weight and height used for the calculation of the body mass index (BMI = weight/height²). Height was measured with a stadiometer attached to the Welmy 200 scale with precision of 0.5cm with the cursor attached in order to facilitate the reading. Height was determined by the placement of the patient barefoot on the stadiometer base, erect posture, feet united, upper limbs relaxed along the body and touching the posterior surface of the body on the measurement scale.

The body weight measurements were performed using a Welmy lever scale with precision of 100g and at the moment of this measurement, the patient was barefoot and wearing minimal clothes as possible. In order to have the measurement taken, the patient was asked to be in the middle of the scale platform, be erect, and have arms along the body and look to the front so that no oscillation occurred during the measurement. The scale was calibrated before the beginning of the weighing and at every 10 weighing procedures.

Waist was measured in cm, with a non-elastic measuring tape, in the mean point between the iliac crest and external surface of the last rib. Hip was measured in centimeters with a non-elastic measuring tape at the level of the anterior iliac spines. The waist/hip ratio (WHR) was obtained by the quotient between the waist and hip circumferences.

Metabolic parameters were evaluated with collection of blood samples observing 12-hour fasting. The dosing performed was the following: fasting glycemia, triglycerides, total cholesterol, HDL-cholesterol and LDL-cholesterol. All biochemical doing was performed with specific commercial kits using the colorimetric enzymatic method according the manufacturer's recommendations.

The statistical comparisons were performed between the sedentary and active groups through the GraphPad Prism (Graphpad, San Diego, CA, USA) program using the Student's *t* test. *P* < 0.05 values were considered statistically significant.

RESULTS

A total of 65 patients were evaluated. Out of these, 23 (35.4%) were considered active (A) by the Baecke questionnaire and 42 (64.6%) were considered sedentary (S). The sociodemographic data are presented in table 1. Regarding sex, 40 (61.5%) were male and 25 (38.5%) were female. Women's age ranged between 26 and 64 years (mean of 42 years) and men's ranged between 20 and 56 (mean of 40 years).

Concerning education, 73.8% had an elementary school diploma, 23% had a high school diploma and 3% had never gone to school. Lower educational level was observed in the female sex, 74% only had an elementary school diploma, while 34% of the male sex had the same educational level.

The data obtained for the waist/hip ratio (WHR) shown in table 2 were analyzed according to the classification proposed by Heyward and Stolarczyk¹⁵. In the two groups, A and S, higher percentage of individuals presented moderate and high risk and no significant difference between groups was observed.

The results of the evaluation of fat percentage were classified according to the classification proposed by Pollock and Wilmore¹⁶ and did not present results with significant difference between groups (table 3).

Table 1. Distribution of the studied population frequency according to its sociodemographic characteristics (n = 65).

Characteristics		Sedentary (n = 42)		Active (n = 23)	
		n	%	n	%
Sex	Male	25	57.1	15	65.2
	Female	17	40.5	8	34.8
Age	< 30 years	7	17.0	2	8.7
	> 30 years	35	83.0	21	91.3
Education	Elementary school	30	71.4	18	78.3
	High school	10	23.8	5	21.7
	Did not study	2	4.8	0	0

Table 2. Classification of the waist/hip ratio of the individuals with HIV/AIDS divided according to the Baecke questionnaire in sedentary and active subjects.

Classification of risks	Active (n = 23)		Sedentary (n = 42)	
	n	%	n	%
Low	4	17.4	6	14.3
Moderate	8	34.8	18	42.9
High	7	30.4	10	23.8
Very high	4	17.4	8	19

Classification of risks according to Heyward and Stolarczyk, 1996.

Regarding the biochemical examinations, the glycemia alterations occurred in three active patients (13%) and in three sedentary patients (7.1%).

Alterations in the lipids levels are presented in table 4. The alterations were considered statistically significant for the HDL-cholesterol; 34 (81%) sedentary patients and 16 (69%) active patients presented undesirable levels. Concerning the blood triglyceride levels in the S group, 14 (33%) and in A group, six (26%) patients presented values above the reference values, but no statistically significant difference was observed.

Concerning the TCD4+ lymphocytes count, 71.4% presented values above 200 cells/mm³ and 28.6% values equal or below, with no difference between groups.

The interviews concerning leisure before and after the HIV infection evidenced in both groups significant alteration in leisure practices with higher prevalence of "watching TV", "house chores", "visiting family", "being alone" and "going to church".

Table 3. Classification of the fat percentage in HIV/AIDS patients divided according to the Baecke questionnaire in sedentary and active subjects.

Fat percentage	Sedentary (n = 42)		Active (n=23)	
	n	%	n	%
Excellent	10	23.8	3	13
Good	3	7.1	3	13
Above average	10	23.8	4	17.4
Average	8	19.2	5	21.7
Below average	1	2.3	3	13
Bad	8	19.2	1	4.3
Very bad	2	4.6	4	17.4

Classification of the fat percentage according to Pollock & Wilmore, 1993.

Table 4. Prevalence of hypercholesterolemia and hypertriglyceridemia in HIV patients who use HAART classified according to the levels of physical activity by the Baecke questionnaire.

Levels of physical activity	Total cholesterol (> 200mg/dL)		LDL-cholesterol (> 100mg/dL)		HDL-cholesterol (> 50 mg/dL)		Triglycerides (> 200mg/dL)	
	n	%	n	%	n	%	n	%
Sedentary N = 42	11	26	19	45.2	34	81	14	33.3
Active N = 23	6	26	9	39	16*	69*	6	26.1

*p < 0.005.

DISCUSSION

Many studies have tried to correlate the metabolic alterations found in HIV/AIDS patients and the HAART; however, few studies have tried to correlate these alterations with the life habits of these patients.

The aim of this investigation was to evaluate the correlation between the levels of habitual physical activity and metabolic parameters in HIV/AIDS patients who use HAART.

Sixty-five patients were evaluated with minimum time of use of HAART of five years and mean of seven years. The patients separated according to the levels of physical activity, sedentary (S) and active (A) ones, were evaluated concerning their fat percentage and waist/hip ratio (WHR) for information about the fat distribution and evaluation of cardiovascular risk. The results obtained with these evaluations (tables 2 and 3) showed that there is no significant difference between groups concerning these parameters.

These results corroborate studies which point the HAART as

an important alternative which enables longer survival to patients. However, its use leads to the onset of the metabolic syndrome associated to the HIV (HIVLS), which adds up to metabolic and cardiovascular risks³. Another metabolic alteration found in HIV patients is the lipodystrophy syndrome (LDS) known as fat redistribution syndrome, leading to fat accumulation in the dorsocervical (buffalo hump) and abdominal regions. This fat redistribution with abdominal lipohypertrophy predisposes to risk of cardiovascular diseases, due to the visceral fat direct association with higher incidence of serum lipid alterations as well as insulin resistance, increasing hence the risk of development of type 2 diabetes¹⁸.

Kramer¹⁹ reported dyslipidemia in the HIV patient who makes use of HAART characterized by increased VLDL (the greatest triglyceride transporter) and LDL-cholesterol levels and reduction of the HDL-cholesterol level. The authors also suggest that the facts which would lead the HIV patient to present dyslipidemias are not totally elucidated yet. It is not clear whether it directly occurs due to the use of HAART or if it is a product of many factors such as: antiretroviral treatment, genetic predisposition, diet and physical exercise or other factors such as the host response to the infection by the HIV.

Farhi²⁰ carried out a study in the University Hospital of Rio de Janeiro with 268 HIV patients and came to the conclusion that in the male patients the prevalence of dyslipidemia is higher when compared to the female sex; and the dyslipidemia family history is directly related to the onset of dyslipidemia and the time of use of the HAART by the patients.

The investigation by Silva *et al.*²¹, carried out in São Paulo, SP, with 319 HIV patients divided in HAART users and non-users, showed that the concentrations of total cholesterol, triglycerides and glucose were statistically higher among patients who made use of HAART. These data suggest higher prevalence of metabolic alterations, especially high levels of triglycerides and cholesterol in patients treated with the drug HAART.

In our study, the time of use of the HAART was standardized in minimum of five years, allowing hence better evaluation of the effect of associated risk factors, namely, the level of physical activity.

The study by Almeida²² observed significant increase in total cholesterol, triglycerides and glucose in 110 patients after the treatment with the HAART. The glucose levels were increased due to the HAART in this study. Nevertheless, in this study, sex, smoking, use of intravenous drugs and age did not significantly influence on the levels of total cholesterol, triglycerides and glucose during the treatment.

Some studies report that exercise and physical activity are benefic to individuals living with HIV, improving their physical ability to control infections²³⁻²⁵. Some authors also report that exercise and physical activity may be positive to HIV patients reducing central and peripheral obesity which is associated with the HAART²⁶⁻²⁸. Improvement in physical conditioning with physical activity and exercise represents better levels of actual energy for activities including leisure activities.

When the laboratory parameters of the patients were evaluated, significant difference between S and A was found concerning the HDL-cholesterol levels. In the remaining parameters (fasting glycemia, total cholesterol, LDL-cholesterol and triglycerides), although differences between the percentages have been observed, they were not statistically significant (table 4).

Although the greatest attention of the metabolic alterations in HIV patients is given to the collateral effects of the HAART, investigation before the HAART era established that the HIV infection itself would determine a more unfavorable lipid profile with hypertriglyceridemia and low HDL-cholesterol. Constans *et al.*²⁹ actually observed prognostic implication of these alterations. The lower the TCD4+ lymphocytes count, the higher the triglycerides level and the lower the HDL-cholesterol levels. The physiopathology of this association is not clear, and the ways through which the antiretroviral therapeutics boosts this lipid disorder and leads to others associated to it, such as increase in insulin resistance, diabetes mellitus, lipodystrophy and centripetal obesity are acknowledged.

Carr *et al.*³⁰ proposed a theory based on the finding of structural homology between the catalytic site and the HIV protease and human proteins, important in the lipid metabolism (CRABP-1: cellular retinoic acid-binding protein 1; and LRP: LDL-receptor related protein) in a way that the antiretroviral of the protease inhibitors class would also inhibit important stages of the human metabolism, contributing to the greater release of fat in the blood. Thus, the protease inhibitors would be blocking the metabolization of the retinoic acid, inducing to lower activity of PPAR- γ (*peroxisome-proliferator-activated receptor type gamma*) plays an important role in the differentiation of adipocytes and in the apoptosis of these cells, besides improving the peripheral sensitivity to insulin. The LRP inhibition on its turn, implies in lower acquisition of triglycerides by the liver and their lower cleavage, which should occur by activity of the endothelial complex of the LRP-LPL (lipoprotein lipase).

In our study it was observed that the alterations in the blood levels of LDL-cholesterol were high regardless of the levels of physical activity, which agrees with the authors mentioned above who explain these alterations as a consequence of the interaction between the HIV infection and antiretroviral drugs, especially the protease inhibitors.

On the other hand, the HDL-cholesterol, whose levels were significantly different in the two groups of patients, have been extensively studied and related to physical activity.

According to some investigations, such alterations are due to the influence of physical exercise on the activity of the lipoprotein lipase enzyme, which is increased in the active individuals³¹⁻³⁴.

Classical studies show that decreased blood HDL-cholesterol levels increase the risk of developing coronary arteriosclerosis^{35,36}.

Hsue *et al.*³⁷ retrospectively evaluated the risk factors and the clinical evolution of 68 HIV patients hospitalized between 1993 and 2003 by unstable angina or myocardial infarct and compared the characteristics of this population with a control group of 68 seronegative individuals with diagnosis of acute coronary arterial disease. Prevalence of smoking and low HDL-cholesterol was higher among the seropositive subjects, while in the control group the presence of diabetes and dyslipidemia was higher. Moreover, the rate of clinically presented stenosis was higher in the seropositive patients and 29 angioplasties were performed in the seropositive patients, while in the control group only 11 were performed. Likewise, it can be suggested that low levels of physical activity and low HDL-cholesterol may be significant factors of cardiovascular risk in HIV patients.

Research related to quality of life of individuals living with HIV/AIDS presents significant results concerning reduction of stress and

its positive correlation with the TCD4 cells count. Ramirez-Marrero *et al.*³⁸ observed this fact in the correlation between physical activities and leisure activities with body composition of hispanic HIV patients. The authors tried to compare the body composition, TCD4 cells count, leisure moments and life satisfaction of patients classified as physically active and inactive. The participants considered active presented higher scores of life satisfaction and healthy body composition compared with those physically inactive.

The instruments of this study presented limitation to compare these elements concerning this aspect. The findings only suggest decrease of physical exercises after the AIDS manifestation. Those who had habitual physical activity, especially in house chores and daily tasks, did not present sedentarism. The results suggest the need to establish strategies which promote health in individuals in that biopsychosocial suffering condition.

FINAL CONSIDERATIONS

Despite the current expressive increase of survival of HIV patients with the use of the HAART, consequent higher association

between metabolic alterations in HIV patients and cardiovascular diseases is observed.

Our study suggests a direct correlation between level of physical activity and better levels of HDL-cholesterol in HIV/AIDS patients. The HDL-cholesterol is a lipoprotein of cardiovascular protection and although other evaluated parameters have not shown difference, these results suggest the need of further studies on risk factors and physical activity for HIV/AIDS patients, making intervention proposals specific to these patients possible.

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