Effect of strength training on people with HIV and immunometabolic disorders

Wlaldemir R. dos Santos[1,2], Walmir R. dos Santos[3], Pedro Pinheiro Paes[4], Klaudia E. Tenório Ramos[5], Emerson H. Dantas Botelho[4], Isac A. Ferreira-Silva[3], Valdir de Queiroz Balbino[2,5], Ana P. Morais Fernandes[1]

[1]School of Nursing of Ribeirão Preto. University of São Paulo. Ribeirão Preto Brazil. [2]Biological Sciences Center. University Federal of Pernambuco. Recife Brazil. [3]School of Physical Education and Sport of Ribeirão Preto. University of São Paulo. Ribeirão Preto Brazil. [4]Physical Education Department. University Federal of Pernambuco. Recife. Brazil. [5]Genetics Department. University Federal of Pernambuco. Recife. Brazil.

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Summary

The introduction of highly active antiretroviral therapy (HAART) was able to help to control viral condition in patients living with HIV/AIDS, diminishing virus concentration and increasing T CD4 + cells. However, adverse effects follow the treatment, like lipodystrophy syndrome, characterized by morphological changes in body fat distribution and changes serum lipids and glycides levels, increasing the risk for chronical diseases with cardiovascular effects. Thus, complimentary non-drug practices, as strength training, are essential to treat these patients, helping to improve their immunometabolic condition, leading to a better coping with the disease. The aim of this study was to investigate the influence of a 12-week strength training protocol on immunometabolic system of people living with HIV/AIDS. It is a quasi-experimental study, conducted on 20 patients (16 men), all living with HIV/AIDS using HAART. T CD4 + cell numbers, serum triglycerides, cholesterol (total and fractions) and glycemia were measured before and after training. The data underwent to descriptive statistics using a paired T test, with the significance level set at $p <0.05$.There was a significant increase of 15.4% ($p=0.009$) on T CD4 + cells and, although not statistically significant, reduction on glycemia, total cholesterol and triglycerides and increase on HDL-cholesterol fraction. So, it is suggested that strength training may be effective on immunometabolic condition of people living with HIV / AIDS, increasing T CD4+ cells and controlling serum levels of lipids and glycides.

Key words:
Strength training. Human immunodeficiency virus. Acquired immunodeficiency syndrome. Highly active antiretroviral therapy. Lipodystrophy. CD4-Positive T-lymphocytes.

Efecto del entrenamiento de fuerza en personas con VIH y trastornos inmunometabólicos

Resumen

La introducción de la terapia antirretroviral altamente activa (HAART) ayudó a controlar la condición viral de los pacientes con HIV/AIDS, reduciendo la concentración del virus y aumentando las células T CD4 +. Sin embargo, los efectos adversos acompañan el tratamiento, como el síndrome de lipodistrofia, caracterizada por cambios morfológicos en la distribución de la grasa corporal y de los niveles metabólicos en los lípidos y glicidos séricos, creciendo el riesgo de enfermedades crónicas con impacto cardiovascular. Así, los tratamientos complementarios no medicados, como el entrenamiento de fuerza, son esenciales en el tratamiento de estos pacientes, lo que contribuye en las mejoras inmunometabólicas en esta población, lo que contribuye a hacer frente a la enfermedad. El propósito de esta investigación fue verificar la influencia de un protocolo de entrenamiento de fuerza con duración de 12 semanas en los sistemas inmunometabólicos de personas con HIV/SIDA. Este es un estudio cuasi-experimental, realizado con 20 pacientes (16 hombres), todos con HIV/SIDA usando la terapia HAART, sometidos a un protocolo de entrenamiento de fuerza de 12 semanas. Se tomaron medidas de las variables número de células T CD4 +, niveles séricos de triglicéridos, colesterol (total y fracciones) y glucosa en sangre, antes y después del entrenamiento. Los datos fueron analizados mediante estadística descriptiva, con prueba T pareada y nivel significativo establecido en $p <0,05$. El resultado mostró un aumento significativo en las células T CD4 + en un 15,4% ($p=0,009$), aunque no es estadísticamente significativo, tuve la glucosa en sangre reducida, así como el colesterol total y los triglicéridos, con respectivo aumento de la fracción de colesterol HDL. Por lo tanto, sugerimos que el entrenamiento de fuerza puede ser efectivo en las condiciones inmunológicas y metabólicas de las personas que viven con HIV/AIDS, aumentando las células T CD4 + y controlando los niveles de lípidos y glucosa en sangre.

Palabras clave:
Entrenamiento de fuerza. Virus de inmunodeficiencia humana. Síndrome de inmunodeficiencia adquirida. Terapia antirretroviral altamente active. Lipodistrofia. Linfocitos T CD4-positivos.

Correspondencia: Wlaldemir Roberto dos Santos
E-mail: wlaldemir@hotmail.com

Introduction

The Human Immunodeficiency Virus (HIV) is a human retrovirus that affects T-helper cells that have CD4 receptor, which are responsible for the immune response. Its infection causes an immunological impairment that leads to AIDS (Acquired Immunodeficiency Syndrome), which has the characteristics of multiple opportunistic infections and several rare diseases[1].

Several treatment improvements made possible the introduction of Highly Active Antiretroviral Therapy (HAART) that modifies the viral action on the body, changing the condition from lethal to chronic, helping to reduce viral load and to maintain CD4+ cells levels[2]. However, HAART has adverse effects, among them, the lipodystrophy syndrome, that is characterized by bad distribution of body fat and metabolic changes[3].

Changes in body fat are classified as lipohipertrophy, lipoatrophy and mixed lipodystrophy Lipohipetrophy is characterized as an increase in abdominal, thoracic and cervical fat, lipoatrophy as a decrease of fat in superior and inferior limbs as well as in face, while lipodystrophy is characterized by both manifestations[4-6]. Generally, these morphological changes do not affect health[5,6]. However, the metabolic changes caused by lipodystrophy start serum lipidic and glycidic variations, increasing the risk to chronic diseases with cardiovascular implications[6]. Lifestyle may influence lipodystrophy, and so, alimentary control and exercises may contribute positively on the manifestation and treatment of this syndrome.

HAART is aimed to control/increase the immunological system (CD4+ T-cells), since its deprivation key to the development of AIDS[1] and lifestyle changes are essential to diminish adverse effects as lipodystrophy syndrome[7].

So, complimentary non-drug practices that control T CD4 + cells are very important to help HAART to control the disease[8]. Among the complimentary therapies to HIV treatment, the regular exercise is one of the most important[9,10], since it may influence directly on the increase in T CD4 + cell numbers besides contributing to control serum lipids and glycemia.

Strength training has been widely used on people living with HIV/AIDS, because it has an important effect on lipodystrophy syndrome[11]. However, few studies demonstrated the effects of strength training on immunometabolic systems on this population. Thus, evidencing the effectiveness of therapeutic resources complementary to HAART are fundamental in coping with the disease, such as strength training in immunometabolic conditions, with a view to positively impacting the longevity and quality of life of these patients. Thus, in a short period (12 weeks), the study aimed to assess the effectiveness of strength training on changes in immunometabolism in people living with HIV / AIDS.

Material and method

It has been a quasi-experimental study, carried out in a continuous flow strength training program initiated in 2013, at the Clinics Hospital from Ribeirão Preto School of Medicine of University of São Paulo (HCFMRP-USP) and at the Guidance and Education Center for Adults and Elders from Nursery School of Ribeirão Preto of University of São Paulo (COEAI/EERP-USP), supported by São Paulo Research Aid Foundation (FAPESP), grants 2011/7300-4 and 2011/03136-5. The study was approved by the Ethics Research Committee from HCFMRP-USP (protocol - 6692/2010), and all subjects signed the free consent form to state the agreement to participate voluntarily on the study, and free to quit at any moment.

The sample was composed by 20 subjects, from both sexes, HIV-positive diagnostic, under HAART for at least 12 weeks. The subjects were between 35 and 70 years old, accompanied at HCFMRP-USP ambulatory and in a nutritional counseling program at the same institution. The subjects were not allowed to use nutritional supplements or other medication beyond HAART and antihypertensive and should not have practiced regular physical exercise for at least three months and should be able to do so, specifically strength training, with a written cardiologic allowance. All subjects not that not fit in the inclusion criteria, had any clinic changes during the training period or had more than 25% absences in the training sessions (9 of 36 sessions) were excluded from the study.

The subjects were recruited among 112 patients, from both sexes (86 males), that were clinically followed at HCFMRP-USP and were included on the nutritional program offered by the hospital. The subjects were invited during the medical advisement or by telephone. From the 112 patients, 97 were contacted and 48 agreed in participate of the training program. Among then, 13 were excluded because they did not fit in the inclusion criteria and three quitted before start training. Thus, 32 subjects begun the training program and, among them, 12 were excluded for absence criteria. The final sample were composed by 20 subjects (16 males), characterized at Table 1.

The strength training was composed of 36 sessions (12 weeks), during 40 minutes (between 2 pm and 5 pm) every Monday, Wednesday and Friday, allowing 48 to 72 hours intervals[12]. In all training sessions, the subjects were under supervision of three researchers involved in the study, all of them physical educators. The 36 sessions were divided in three consecutive phases: 1) preparation, six sessions with three series of 15 repetitions and a 60 seconds interval between exercises[12], with intensities determined according to Borg scale[13] ranging from 11 (fairly light) to 13 (somewhat hard); 2) adaptation, six sessions with three series of 15 repetitions and 60 seconds intervals between exercises, intensities ranging from 40 to 50% of the obtained at the maximum repetition test – 1MR[12]; 3) specific, 24 sessions with three series of with 8 repetitions and 90 seconds intervals, with intensities ranging from 70 to 80% of 1MR[12]. Based on the basic principles for periodization and physical exercise prescription[14] and due to the natural adaptation to physical exercise, at the end of the 12nd session of the specific period (total of 24 sessions), a new 1MR test was applied to readapt the training load intensity, still fixed at 70-80% of 1MR[12].

Strength training was composed by the following exercises (following the respective order): warm up (active stretching), supine, pull back, knee extension, knee flexion, elbow extension, abdominals, plantar flexion and relaxation (active stretching)[12].

Before each session, the subjects were questioned and evaluated for the general health status, vital signs measured (arterial pressure, heart rate, breath rate and oxygen saturation), repeated after the training. During training sessions, the subjects were oriented and monitored to rehydration with water between the exercises series and had their clinical condition monitored. Any clinical instability before, during or after the training sessions were considered as an exclusion criteria and the subject were sent to medical care at HCFMRP-USP. The subjects were oriented about the importance of resting and sleeping between the training session.

Personal data as age, viral infection period, training time and medication used were collected using a questionnaire applied before the beginning of the training protocol, all data confirmed at their medical records. Body weight and height were measured using a scale (Welmy), intervals of 0.1 kilograms (kg) and 0.1 centimeters (cm).

Before and after the training program (36 sessions - 12 weeks) were measured the number of CD4+ T-cells, serum levels of triglycerides, total, HDL and LDL cholesterol (lipogram) and blood glucose. Lipogram analysis and blood glucose were made using the enzymatic method and the CD4+ T-cells count were obtained using Flux Cytometry (ACEA Biosciences).

Exams were collected during the routine examination at HCFMRP-USP. A maximum period of three months before the initial evaluation of this study was considered to accept the data from exams. If the patient did not have results in this period, a requisition for new exams were given to get them. After the training period, the patients received another requisition for post training exams.

The strength training protocol was conducted in equipment station (Athletic Way) with two independent 180 kg columns, allowing two patients to exercise at the same time. To determine the initial training intensity, the preparatory phase, the Borg scale were used[13]. This phase aimed to teach the correct movements, considering the efforts as fairly light and somewhat hard. The patients were oriented to point the physical effort at Borg scale, when the pointed value did not fit the expected interval, the training load were adjusted[12]. In all sessions of this phase, the patients were corrected to execute the right movements, at the right body position, movement amplitude and corrected breathing.

After learning the movement in the prior stage, the patients were submitted to 1MR test, to determine training intensity in the subsequent stages, this test was already used in people living with HIV[15-17]. This test was used in three moments: before the adaptation stage, in the middle of this specific stage (12 sessions, to readjust the intensity) and at the end of the training program. This test aims to register the maximum weight that the subject is able to execute a single repetition with the movement complete amplitude. The subjects were tested progressively, the load were increased until the subject were not able to complete the needed amplitude, then the previous load was registered as the maximum load[12,17]. However, only six attempts were made, in 80 seconds intervals between the attempts, if the 1MR were achieved, a new test were conducted after 72 hours[12]. Plantar flexion was conducted unilaterally on the floor and was not tested for 1MR.

A Shapiro-Wilks normality test was used to determine if the data were normally distributed. The sample was characterized by a descriptive analysis with the means, maximum and minimum values for age, body weight, height, infection time, HAART use, viral load and therapeutic regimen. Immunological and metabolic changes were measured pre and post training, then the data were analyzed through a paired T-test, using SPSS 13.00 software, with significant level set at $p < 0.05$. The calculation of the effect size was performed using the Cohen formula and the results were based on the following criteria: negligible effect (> = -0.15 and <.15), small effect (> =. 15 and <.40), medium effect (> =. 40 and <.75), large effect (> =. 75 and <1.10), very large effect (> = 1.10 and <1.45) and huge effect > 1.45.

Table 1. Sample characterization of trained group.

Variable (n=20)	Mean (min-max)	CI (95%)
Age (years old)	50.6 (38.0-67.0)	46.895 to 54.305
Weight (kg)	71.8 (51.1-111.2)	65.386 to 78.233
Height (cm)	169.3 (151.0-185.0)	165.352 to 173.198
HIV Infection Time (years)	11.3 (1.0-23.0)	8.147 to 14.453
HAART Use (years)	9.8 (1.0-23.0)	6.648 to 12.951
IP Use, n (%)	15/20 (75.0)	0.673 to 1.527
ITRAN Use, n (%)	19/20 (95.0)	1.336 to 1.964
ITRNN Use, n (%)	10/20 (50.0)	0.260 to 0.740
Training Frequency (%)	90 (81-100)	1.57 to 8.44

IP: Protease Inhibitors; ITRAN: Nucleoside Analogues Reverse Transcriptase Inhibitors; ITRNN: Nucleoside Non-Analogues Reverse Transcriptase Inhibitors.

Result

There were 20 subjects in this study (16 males) with the mean age of 50.6 years old, mean weight of 71.8 kg and mean height of 169.3 cm. As to infection time, the subjects were infected for 11.3 years (mean infection time), using HAART for 9.8 years, 15 individuals (75%) use protease inhibitors (IP), 19 (95%) use nucleoside analogues of reverse transcriptase inhibitors (ITRAN) and 10 (50%) nucleoside non-analogues of reverse transcriptase inhibitors (ITRNN; Table 1).

As to immunological response, we found that, after the proposed protocol, the individuals showed a significant increase of 69.2 (15.4%; p=0.009) cell/µl in CD4+ T-cells. Regarding the metabolic conditions, we observed increase in HDL-cholesterol of 1.4 (3.9%) mg/dl and LDL-cholesterol of 1.5 (1.3%) mg/dl, decrease of serum triglycerides of 38.4 (16.9%) mg/dl, total cholesterol (14.7 mg/dl; 7.4%) and blood glucose of 4.8 (4.9%) mg/dl,

however, metabolic responses were not statistically significant. Regarding the size of the effect, a medium result (0.47) in the levels of trliglycerides was found significantly (Table 2).

Discussion

The control of the viral condition is very important to evaluate clinical appearance of HIV. HAART acts changing viral action on the body, helping to reduce viral count and maintaining CD4+ T-cells[2]. Nevertheless, HAART has adverse effects, as lipodystrophy syndrome, that leads to changes in metabolic lipids rate and insulin resistance, which may lead to chronical diseases with cardiovascular risks[3,6].

Since the longevity of people living with HIV/AIDS is increasing consistently, it became vital the development of therapies that help

Table 2. Immunological and metabolic responses after 12 weeks of training.

Parameter		Descriptive Mean (min-max)	Paired differences Diff mean (%) Effect size (result)	T	df	*p*
Trained group						
Lymphocytes T CD4+ (cell/µl)	Pre	449.8 (105.0-1073.0)	69.2 (15.4) 0.27 (small)	-2.8936	19	0.009*
	Post	519.0 (105.0-975.0)				
Triglycerides (mg/dl)	Pre	227.4 (95.0-521.0)	-38.4 (16.9) 0.47 (medium)	1.9192	19	0.070
	Post	189.0 (95.0-361.0)				
Total cholesterol (mg/dl)	Pre	197.2 (125.0-313.0)	-14.7 (7.4) 0.38 (small)	1.6363	19	0.118
	Post	182.5 (125.0-247.0)				
HDL Cholesterol (mg/dl)	Pre	35.74 (26.0-50.0)	1.4 (3.9) 0.21 (small)	-1.014	19	0.323
	Post	37.15 (26.0-54.0)				
LDL Cholesterol (mg/dl)	Pre	115.7 (75.0-221.0)	1.5 (1.3) 0.03 (negligible)	-0.1009	19	0.920
	Post	117.2 (72.0-266.0)				
Glycemia (mg/dl)	Pre	99.70 (79.0-165.0)	- 4.8 (4.9) 0.29 (small)	1.1231	19	0.275
	Post	94.85 (74.0-146.0)				

HAART on the control of CD4+ T-cells and, among the complementary therapies to the medication, the regular physical exercise is one of the most important[9,10], acting either in increasing CD4+ T-cells and controlling metabolic changes, those changes can increase the life spam for these individuals[18]. Strength training has been used as a complementary therapy in people living with HIV/AIDS[11]. However, few studies issue the effects of strength training on the viral condition of these population.

In the present study, the efficiency of strength training over the immunological and metabolic conditions in people living with HIV/AIDS. The proposed training protocol (12 weeks) were efficient in increasing the CD4+ T-cells by 15.4% (p=0.009). This increase can be influenced acute and chronically by exercise. The stimuli caused by the training recruits white cell subpopulations to the vascular lumen, as CD4+ T-cells, which remain slightly elevated after the exercise, increasing its concentration in result of chronic exercise[19].

Our results are in agreement to Zanetti *et al.*[20], who evaluated the efficiency of a 12 weeks strength training observing a significant increase in CD4+ T-cells (p=0.004), similar results were found by Anandh *et al.*[21] (p=0.041). On the other hand, in a case study with one man and one woman, Mesquita Soares *et al.*[22], found a decrease in the man and a increase in the woman on CD4+ T-cells, questioning the efficiency of the strength training on people living with HIV/AIDS. The number of subjects may be too small to observe the effect seen on this study, which presents the same results found in the systematic review conducted by Pedro *et al.*[23].

When we verified the metabolic responses to the strength training, we did not find any significant changes, however, the study showed strong evidence that strength training contributes to the metabolic changes seen in lipodystrophy syndrome, since the protocol adopted increased HDL-cholesterol (3.9%) and LDL-cholesterol (1.3%), reduced triglycerides (16.9%), total cholesterol (7.4%) and blood glucose (4.9%). Terry *et al.*[24] also showed no significant changes on metabolic parameters after strength training in people living with HIV/AIDS. However, Mendes *et al.*[25] demonstrated, in a 12 weeks duration strength training protocol, reduction of serum triglycerides (9.9%), total cholesterol (12.0%), LDL-cholesterol (8.6%) and an increase in HDL-cholesterol (16.7%). Robinson *et al.*[26] demonstrated that a 16 weeks strength training protocol reduced serum triglycerides (59 mg/dL; p=0.001) and insulin resistance (15.7%; p=0.001).

From the literature review carried out, we identified few studies that verified the effectiveness of strength training on immunometabolic variables in people living with HIV / AIDS. In this research, the authors understand as a limitation the fact that it was not possible to perform the sample calculation, due to the difficulty in recruiting patients with the profile necessary for the study, the sample being selected from 112 patients who were undergoing clinical and nutritional monitoring at HCFMRP-USP. Added to the fact that the nutritional monitoring carried out does not have a strict control in the domestic context, since the prescriptions made by the professionals were not controlled outside the hospital. In a complementary way, the findings of this study (except for the limitations of the study presented here) provided reflections on the disease and complementary non-drug therapeutic measures for the immunometabolic control of HIV / AIDS. However, the findings discussed here could only be generalized to other contexts based on strict dietary control (not addressed in the present study) and the faithful reproduction of the physical exercise protocol.

Thus, we observed that strength training can be effective on the immunological and metabolic conditions of people living with HIV/AIDS. It has an important role increasing CD4+ T cells, thus being a fundamental not-medicated treatment in this population. Strength training can also control serum levels of triglycerides, total and fractions cholesterol and the blood glucose, we propose that training protocols longer than 12 weeks can be effective to this effect. Thus, strength training may be a complementary resource to fight HIV/AIDS, however, it is suggested that further studies may be needed to detect the most effective time and protocols of strength training.

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Conflict of interest

The authors do not declare a conflict of interest.

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