Impact of strength training on bone mineral density in HIV-positive patients

Impacto do treinamento de força na densidade mineral óssea em pacientes HIV positivo

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Abstract

Introduction: Highly active antiretroviral therapy (HAART) transformed HIV from a fatal disease to a chronic one, but it has adverse effects, such as the lipodystrophy syndrome, characterized by morphological and metabolic changes, such as reduced bone mineral density (BMD), potentiating morbidities and mortality. Strength training (ST) aims to increase BMD, due to the osteogenic effect. **Objective:** To verify the impact of strength training on BMD in people with HIV. **Methods:** This is a quasi-experimental study, which included 40 people with a mean age of 50 ± 6 years, separated into trained group (TG, n = 20) and control group (CG, n = 20), with reduction in BMD, HIV-positive, using HAART and without exercising. BMD was assessed by DEXA in the lumbar spine, femoral neck and distal 1/3 of the radius, before and after 12 weeks, with the GT submitted to 36 ST and the CG without physical training in the DEXA evaluation in the same time interval. **Results:** TG had a significant increase with great effect on BMD in all segments: lumbar spine (p = 0.001; ES: 1.87), femoral neck (p = 0.003; ES: 2.20) and 1/3 distal of the radius (p = 0.001; ES: 1.81). Meanwhile, CG group showed a significant reduction with great effect on the femoral neck (p = 0.020; ES: 2.56) and 1/3 distal of the radius (p = 0.015; ES: 2.93), while the lumbar spine showed a great effect to reduce BMD (p = 0.293; ES: 1.78). **Conclusion:** ST can be used as a therapeutic resource to increase BMD in people with HIV, contributing to the advancement in the search for non-drug therapeutic practices.

Keywords: Bone density. HIV associated lipodystrophy syndrome. Resistance training.

Resumo

Introdução: *A terapia antirretroviral altamente ativa (HAART) transformou o HIV em uma doença crônica, apresentando efeitos adversos como a síndrome da lipodistrofia, caracterizada por alterações morfológicas e metabólicas, como redução da densidade mineral óssea (DMO), potencializando morbidades e mortalidades. O treinamento de força (TF) tem como proposta aumentar a DMO, devido ao efeito osteogênico.* ***Objetivo:*** *Verificar o impacto do TF na DMO em pessoas com HIV.* ***Métodos:*** *Trata-se de um estudo quase-experimental que incluiu 40 pessoas com idade média de 50 ± 6 anos, separadas em grupo treinado (GT, n = 20) e grupo controle (GC, n = 20), com redução na DMO, HIV positivo, usando HAART e sem praticar exercícios físicos. A DMO foi avaliada pelo DEXA na coluna lombar, colo do fêmur e 1/3 distal do rádio, antes e após 12 semanas, com o GT submetido a 36 sessões de TF e o GC sem exercício durante o mesmo período.* ***Resultados:*** *O GT teve aumento significante com grande efeito em todos os segmentos: coluna lombar (p = 0,001; ES: 1,87), colo do fêmur (p = 0,003; ES: 2,20) e 1/3 distal do rádio (p = 0,001; ES: 1,81), enquanto o GC apresentou redução significante com grande efeito no colo do fêmur (p = 0,020; ES: 2,56), 1/3 distal do rádio (p = 0,015; ES: 2,93) e apenas grande efeito na coluna lombar (p = 0,293; ES: 1,78).* ***Conclusão:*** *O TF pode ser utilizado como recurso terapêutico para aumentar a DMO em pessoas com HIV, contribuindo para o avanço nas buscas de práticas terapêuticas não medicamentosas.*

Palavras-chave: *Densidade mineral óssea. Síndrome de lipodistrofia associada ao HIV. Treinamento de força.*

Introduction

The introduction of highly active antiretroviral therapy (HAART) was able to transform HIV/AIDS from a lethal to a chronic disease.[1] However, adverse effects affect patients, such as the lipodystrophy syndrome, which is characterized by morphological and metabolic variations,[2] highlighting changes in calcium deposition.[3]

Changes in calcium deposition lead to a reduction in bone mineral density (BMD), making osteopenia and osteoporosis common among those patients,[3-5] which are enhanced by the development of the disease, lifestyle[5] and genetic factors.[6] As a result, the reduction of BMD becomes a serious problem for patients with HIV, due to the high rate of morbidities and mortality associated with fractures, directly impacting the longevity and biopsychosocial conditions of patients.[5,7]

Some studies use calcium replacement and vitamin D as a complementary resource to the treatment of HAART, minimizing the damage in BMD.[5] As a non-pharmacological therapeutic resource, changes in lifestyle through physical exercise have been well used for these patients.[8] In particular, strength training has shown a positive response in increasing BMD in HIV-positive patients.[9]

Strength training is a great resource to increase BMD, as its mechanical characteristics lead to a greater osteogenic effect, contributing to the health of patients.[10] However, studies are still scarce with this population, requiring more research to encourage the applicability of strength training as a treatment complement to HAART in people with HIV. Thus, the present study aimed to verify the impact of strength training on BMD in people with HIV.

Methods

This is a quasi-experimental study,[11] lasting 12 weeks, held at the Education and Orientation Center for Adults and Senior Citizens of the Ribeirão Preto Nursing School, Universidade de São Paulo (COEAI/EERP - USP), in Ribeirão Preto, SP, Brazil.

After approval by the Research Ethics Committee of HCFMRP-USP (Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto; protocol 6692/2010), all subjects signed a free research informed consent form agreeing to participate in the study voluntarily and aware that they could leave it at any time. This investigation was funded by the São Paulo State Research Support Foundation (FAPESP), processes 2011/7300-4 and 2011/03136-5. Subjects were over 18 years old, had a positive diagnosis for HIV/AIDS, were using antiretroviral therapy, had lipodystrophy syndrome and reduced bone mineral density (confirmed by bone densitometry), did not undergo hormone replacement and/or calcium supplementation, had not practiced regular physical exercise for at least three months, and had the authorized cardiological opinion that they were able to do physical exercises. Subjects who had any clinical instability during training, who had attendance lower than 75% of training sessions, or who began physical exercise during the

12-week interval in addition to the protocol stipulated for the trained group (TG) were excluded.

The 112 patients who were being followed up at the infectious diseases sector at HCFMRP-USP were contacted by phone or in person during medical consultations and invited to the study. Of these, 48 agreed to participate in the study, thirteen of which were excluded for not meeting the inclusion criteria and three dropped out before starting the training protocol. Thus, 32 patients started the training program and, of these, twelve were excluded for not attending 75% of the sessions, claiming lack of time to attend training sessions, which did not have the post-training variables analyzed, leaving the final sample with 20 subjects forming the TG.

The control group (CG) consisted of 20 patients who met the aforementioned inclusion criteria and did not have time available for training, but agreed to participate in the study by answering an interview to verify their living conditions and performing bone densitometry to monitor BMD for a period of 12 weeks, the same interval performed with the TG, but without physical exercise in the period.

Personal details of the participants, such as age, time of viral infection, time of treatment and drugs used were collected using a questionnaire applied before the beginning of the training protocol for the TG, and in the period corresponding to the interval in the CG. The medical records checked the information collected in the questionnaire, in addition to recording the number of CD4+ cells.

The patients included in this study underwent BMD measurement using dual energy X-ray absorptiometry (DEXA) equipment (Hologic QDR 4500A scanner; Hologic Inc., Waltham, MA, USA), at HCFMRP-USP. The anatomical points collected were the lumbar spine (L1-L4), femoral neck and 1/3 distal radius before and after the strength training protocol.[12] These regions were selected because they have the highest rate of low BMD and are used for the diagnosis of osteoporosis and osteopenia validated as a reference standard according to the World Health Organization.[9,11] The regions evaluated in this study are also cited as reference values for BMD in patients living with HIV.[5,9] BMD values were expressed with the T-score, as it is the absolute value in g/cm^2 compared to the mean bone mass of a healthy young adult, with an upward or downward deviation from the mean, used to predict and classify risk fracture.[9,11] Individuals' body mass and height were measured with a Welmy stadiometer and electronic scale, with a minimum detectable 0.1 kg for body mass and 0.1 cm for height.

The strength training protocol consisted of 36 sessions (12 weeks) of approximately 40 minutes (between 2 pm and 5 pm) every Monday, Wednesday and Friday, with training on alternate days allowing at least 48 hours of rest between sessions (recommended time for recovery between stimuli). In all sessions, patients were under the supervision of three researchers (all of them with a bachelor´s in Physical Education). The 36 sessions were divided into three consecutive phases: preparation - six sessions with three sets of 15 repetitions and 60-second intervals between exercises,[13] the intensity being determined by the Borg and Noble scale,[14] with a score between 11 (almost easy) and 13 (not very tiring); transitional - six sessions with three sets of 15 repetitions and 60-second intervals between exercises, with intensities ranging from 40 to 50% of the result obtained in the test of 1 maximum repetition (1RM);[13] specific - 24 sessions with three sets of eight repetitions and 90-second intervals, with intensities ranging from 70 to 80% of 1RM.[13] Based on the basic principles of periodization and prescription of physical exercise,[15] and as a result of the natural process of adaptation to physical exercise, at the end of the 12th session of the specific period (total of 24 sessions), a new 1RM test was applied to readapt the intensity of the training load, still maintained at 70-80% of 1RM.[13]

After learning the movement in the previous phase, the patients were submitted to the 1RM test to determine the training intensity of the subsequent sessions, the test being performed in three moments: before the transition phase, in the middle of the specific phase (12 sessions) and at the end of the training program period. The 1RM test aims to record the maximum weight that the individual is able to lift in a single repetition with the correct range of motion. The load was gradually increased until the subjects were unable to complete the movement with the necessary amplitude, the previous load being measured.[13,16] This training intensity parameter procedure has been used in other studies involving people with HIV.[9,13,16] However, only six attempts for each exercise were allowed at 80-second intervals. In case it was not possible to identify the value of 1RM, a new test would be performed 72 hours after the end of the previous test.[16] The plantar flexion exercise was performed unilaterally on the ground, but its 1RM was not measured.

Strength training was performed using a training station (Athletic Way) with two independent columns of 180 kg each, supporting the execution of up to two people simultaneously, and composed of the following exercises, in the following order: warm-up (active stretching), bench press, frontal pull, leg flexion, leg extension, elbow flexion, elbow extension, abdominal exercise, plantar flexion and calm back (active stretching). The order of the exercises was designed to initially prioritize the major muscle groups and multi-joint movements, as recommended by Garber et al.[13]

Before each training session, participants were asked about their general health and their vital signs were measured (blood pressure, heart and respiratory rate, and oxygen saturation). During training, the subjects were monitored for rehydration with water and between each series of exercises for clinical conditions. In addition, patients were informed about the importance of rest and sleep between training sessions.

The Shapiro-Wilk normality test was used to determine whether the data were normally distributed. All variables were checked in the baseline, guaranteeing the homogeneity of the groups. The sample was characterized through descriptive analysis with maximum and minimum values for age, body weight, height, time of infection, use of antiretroviral therapy, CD4+ cell count, viral load and therapeutic regimen. BMD of the lumbar spine, femoral neck and 1/3 distal radius was measured before and after the strength training protocol. The data were analyzed by the test of paired samples (inter and intra groups), using the software SPSS 13.00, with significance level set at $p < 0.05$. The calculation of the effect size (ES) was performed using the Cohen formula and the results were based on the following criteria: negligible effect (> = -0.15 and < 0.15), small effect (> = 0.15 and < 0.40), medium effect (> = 0.40 and < 0.75), large effect (> = 0.75 and < 1.10), very large effect (> = 1.10 and < 1.45) and huge effect (> 1.45).

Results

The sample consisted of 40 people (20 in each group), with homogeneous characteristics, 28 men (70%), with an average age of 50 ± 6 years old, body weight of 69.9 ± 9.3 kg and height of 169.2 ± 6.3 cm. Average time of HIV infection was 11 years, the time of use of antiretroviral therapy was 9 years, and the TCD4+ cell count was 488.9 cells/µl, with the data of the sample characterization shown in Table 1. Regarding therapy, 95% of patients used nucleoside reverse transcriptase inhibitors, 75% of patients used protease inhibitors and 50% used non-nucleoside reverse transcriptase inhibitors. In relation to the training attendance, the individuals presented an average attendance of 90% (81 - 100%).

We did not find significant differences in BMD between groups. However, observing intragroup, we verified a significant increase and huge effect in density in all measured segments (lumbar spine, femoral neck and 1/3 distal radius) in the TG, while the CG presented significant reduction in the femoral neck and 1/3 distal radius and huge effect in other regions. In relation to the lumbar spine, the TG increased the BMD T-score by 13.7% ($p = 0.001$; ES: 1.87), while the CG reduced BMD by 35.8% ($p = 0.293$; ES: 1.78); in the femoral neck, the TG increased by 19.5% ($p = 0.003$; ES: 2.20), while the CG decreased by 27.7% ($p = 0.020$; ES: 2.56); on the 1/3 distal radius, the TG increased by 18.0% ($p = 0.001$; ES: 1.81), with the CG having a reduction of 11.7% ($p = 0.015$; ES: 2.93) (Table 2).

Table 1 - Sample characterization

Variable	Total (n = 40)*	Trained group (n = 20)*	Control group (n =20)*
Age (years)	50.0 ± 8.0 (1.000)	50.0 ± 6.0 (1.000)	50.0 ± 7.0 (1.000)
Weight (kg)	69.9 ± 9.3 (0.346)	71.8 ± 10.1 (0.346)	68.0 ± 10.0 (0.346)
Height (cm)	169.2 ± 6.0 (1.000)	169.2 ± 6.0 (1.000)	169.2 ± 8.0 (1.000)
Time of HIV infection (years)	11.0 ± 5.0 (0.860)	11.0 ± 5.0 (0.860)	11.0 ± 5.0 (0.860)
Use of HAART (years)	9.0 ± 5.0 (0.955)	9.0 ± 5.0 (0.955)	9.0 ± 5.0 (0.955)
TCD4 + cells (cells/µl)	488.9 ± 233.8 (0.421)	449.8 ± 225.4 (0.421)	527.9 ± 303.6 (0.421)
Lumbar spine (T-score)	-1.4 ± -1.4 (0.421)	-1.6 ± -1.2 (0.421)	-1.3 ± -1.5 (0.421)
Femoral neck (T-score)	-1.0 ± -1.1 (0.360)	-1.4 ± -0.9 (0.360)	-0.6 ± -1.2 (0.360)
1/3 distal radius (T-score)	-1.6 ± -1.3 (0.107)	-1.9 ± -1.3 (0.107)	-1.2 ± -1.2 (0.107)

Note: *mean ± standard deviation; HAART = highly active antiretroviral therapy.

Table 2 - Bone mineral density (T-score) determined before and after strength training protocol

Variable (T-score)	Group	Baseline[1]	After 12 weeks[1]	Δ (%)	Standard deviation	P (Effect size)	Intergroup P (Effect size)
Lumbar spine	Trained	-1.6 ± -1.2	-1.4 ± -1.2	-0.2 (13.7)	0.11	0.001 (1.87)*	0.638 (0.17)
	Control	-1.3 ± -1.5	-1.7 ± -2.3	0.5 (-35.8)	0.23	0.293 (1.78)	
Femoral neck	Trained	-1.4 ± -0.9	-1.1 ± -1.0	-0.3 (19.5)	0.14	0.003 (2.20)*	0.318 (0.29)
	Control	-0.6 ± -1.2	-0.8 ± -1-1	0.2 (-27.7)	0.08	0.020 (2.56)*	
Femoral neck	Trained	-1.9 ± -1.3	-1.6 ± -1.3	-0.3 (18.0)	0.17	0.001 (1.81)*	0.645 (0.16)
	Control	-1.2 ± -1.2	-1.4 ± -1.2	0.2 (-11.7)	0.07	0.015 (2.93)*	

Note: [1]mean ± standard deviation; *p > 0.05.

Discussion

BMD is a measure that indicates the structure of the bone matrix and its reduction leads to osteopenia and, later, to osteoporosis. Osteoporosis is characterized as an initially asymptomatic disease, of a systemic and skeletal nature, which makes the bone structure weak and susceptible to fractures, affecting mainly the lumbar spine, femoral neck and 1/3 distal radius.[12,17] Studies point to high fracture rates among HIV-positive patients, and as a consequence, increased morbidity and mortality in this population.[3,5,9]

In the present study, for 12 weeks, we followed 40 patients with HIV and reduced BMD. Twenty of these patients (CG) did not undergo any physical exercise and had reduced BMD in the lumbar spine (p = 0.293; ES: 1.78), femoral neck (p = 0.020; ES: 2.56) and 1/3 distal radius (p = 0.015; ES: 2.93), showing that only three months were sufficient for the depreciation of BMD, characterized by the progressive catabolism of lipodystrophy in people with HIV.[18]

During the same period, the other 20 patients (TG) underwent a strength training program, where they obtained a significant increase in BMD in all evaluated structures: lumbar spine (p = 0.001; ES: 1.87), femoral neck (p = 0.003; ES: 2.20) and 1/3 distal radius (p = 0.001; ES: 1.81). During exercises of muscular action against resistance, such as strength training, the bone undergoes mechanical loads due to muscle contraction and gravitational weight discharge, which leads to cellular mechanical stimuli that, with adaptive responses, increases formation and resorption.[8,9,12,19]

In a pioneering study, Santos et al.[9] observed that 20 patients with HIV and lipodystrophy had increased bone mineral density in the lumbar spine (p = 0.012), femoral neck (p = 0.044), and 1/3 distal radius (p = 0.035). Perazzo et al.,[8] evaluating 41 people with HIV before and after 96 weeks of intervention in a guided physical activity program, with predominantly aerobic activities of moderate and high vigor, found an increase in BMD in the femoral neck (p = 0.009) and lumbar spine (p = 0.001). Similar results were found by Watson et al.,[20] who found an increase in BMD in 101 HIV-positive and postmenopausal women in the lumbar spine (p = 0.001) and femoral head (p = 0.004).

Studies with physical interventions to assess BMD in people with HIV are scarce. Observing other populations, we found results similar to the present study. Nickols-Richardson et al.[21] observed an increase in BMD in the femoral neck and 1/3 distal radius in young women submitted to 20 weeks of strength training. In a 12-month case study with a post-menopausal woman undergoing strength training, Aquino et al.[10] noted an increase in BMD in the lumbar spine and femoral neck. Similar results were observed by Avila et al.[22] in 213 soldiers who underwent seven months of impact physical training, increasing BMD in all body segments.

Patients with HIV tend to have a reduction in BMD due to HAART, which results in lipodystrophy.[3] Studies that explore pathophysiological factors and effective therapies for BMD in this population are scarce. However, factors such as virus infection, hormonal changes, vitamin D deficiency and physical inactivity contribute to the condition.[4,5] Some studies state that the handling is the same used for people not infected by HIV (lifestyle change, hormone replacement, calcium and vitamin D intake and physical exercise).[8,9,23]

The present study, although as an experimental approach, obtained extremely significant results in a short period of time, adding to the clinical conditions

of the patients. Thus, experimental studies (double-blind and randomized) could add even more to the subject. Furthermore, we suggest studies that monitor other conditions that may influence BMD responses, such as daily and work activities, variables that were not controlled in this study.

Conclusion

Our results suggest that strength training, for a short period (12 weeks), can be used as a complementary non-medicated treatment to combat progression of bone catabolism, contributing to the increase in BMD in the lumbar spine regions, femoral neck and 1/3 distal radius. Thus, it helps to better cope with the disease, encouraging the practice of strength training as a complementary therapy, contributing to the advancement in the search for non-drug therapeutic practices.

Authors' contributions

Santos WR, Santos WR, Paes PP, Fernandes TM, Tenório KER and Fernandes APM contributed to the study conception and design, analysis and interpretation of results, writing and critically reviewing the manuscript and approving the final version, and are responsible for all aspects of the study, including its accuracy and integrit.

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