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Physical Training on Immunological and Virological Response to HIV Infected Patients

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Abstract

Physical training can be a non-pharmacological intervention to improve the parameters of health-related physical fitness. However, it has not been fully determined its potential influence on virologic and immunologic outcomes yet. The aim of this article is to review the scientific literature on the effects of physical training on immune response and viral load of HIV positive individuals. The research method was based on a systematic review of randomized clinical trials, consisting of articles published between 1999 and 2012 on PubMed, Web of Science, EMBASE, Lilacs and Medline databases. From the outcomes of this systematic review of randomized clinical trials, it is possible to affirm that aerobic and concurrent training with multiple sets, despite being safe, do not interfere in the increase in the immune response and in the decrease in viral load of HIV people living with HIV/AIDS.

Keywords: HIV; AIDS; Physical activity; Immune response; Systematic review

Introduction

The Acquired Immunodeficiency Syndrome (AIDS), the final stage of Human Immunodeficiency Virus (HIV), is regarded as one of the most feared pandemics nowadays. The process of viral replication occurs in cells showing phenotypic marker $CD4^+$ T, mainly lymphocytes which play a major role in the modulation of the immune response [1]. AIDS is characterized by immune deficiency, as a result of the slow and progressive destruction of $CD4^+$ T lymphocytes, usually having a cell count <200 cells/mm3 [2]. In this contest, the measurement of the absolute $CD4^+$ T lymphocytes count, their percentage in relation to total lymphocytes and quantification of HIV in plasma (viral load), constitute the best laboratory predictors of HIV progression to AIDS or, even death [3]. The combination of Highly Active Antiretroviral Therapy (HAART) significantly reduced mortality in people living with HIV/AIDS; however, its prolonged use may be associated with the development of other comorbidities such as lipodystrophy syndrome, defined as the body fat redistribution, and metabolic changes, which increase the risk of cardiovascular diseases [4,5]. Interventions to improve these complications are often needed to reduce morbidity and mortality risks. Physical training could be a non-pharmacological tool in this scenario. While getting better health-related physical fitness parameters, it could also improve the effects resulting from the prolonged use of ART. However, it has not been fully determined its potential influence on virologic and immunologic outcomes yet. The aim of this article is to review the scientific literature on the effects of physical training on immune response and viral load of HIV-seropositive individuals.

Methods

The research method was based on a systematic review of randomized clinical trials (<I>Centre for Evidence Based Medicine, Oxford: www.cebm.net), consisting of articles published between 1999 and 2012 on PubMed, Web of Science, EMBASE, Lilacs and Medline databases. The beginning of the investigation period was determined from the moment the first publications addressing physical activity were found. The keywords and/or their associated terms used for research were: randomized, trial, HIV/AIDS, physical activity, exercise, aerobic, resistance, concurrent, training, viral load, immunology and CD4 cell. It has been shown that randomized clinical trial is the best strategy to test the effectiveness of a new therapy, being possible to identify the effects under controlled conditions of observation [6]. The articles were assessed independently by three assessors according to the following inclusion criteria: (1) HIV/AIDS population (adults), (2) intervention (physical training and (3) outcomes ($CD4^+$ T count and viral load). During the initial selection process, 41 articles were identified and, after reading10 articles remained according to the inclusion/exclusion criteria: 05 on aerobic training and 05 on concurrent training (combination of aerobic and resistance exercise in the same training session) with multiple sets (3

or more sets for each exercise). No studies were found on isolated resistance training and on concurrent training with single set (single set for each exercise).

Results and Discussion

Aerobic training

Five studies on aerobic training were found: Terry, Sprinz and Ribeiro, Perna et al., Smith et al., Baigis et al. and Terry et al. [7-11]. Terry et al. [7] assessed the functional capacity, anthropometric measurements, depression scores and immunologic variables in 21 patients (14 men and 7 women) allocated into two groups: moderate-intensity aerobic exercise (n=10) and high-intensity aerobic exercise (n=11). The study was conducted over 12 weeks at a frequency of 60-minute sessions, three times per week, at an intensity of 60 ± 4% H_{Rmax} (moderate) or 84 ± 4% H_{Rmax} (high). It was observed a significant increase in the functional capacity of both groups, and there was no significant change in the $CD4^+$ T lymphocytes count or viral load. Perna et al. [8] conducted a study with 21 HIV/AIDS subjects (11 in the experimental group and 10 in the control group) who used a medication regimen without the presence of protease inhibitors. Cardiorespiratory function and $CD4^+$ T lymphocytes count were assessed. The aerobic training was carried out 3 times per week, with approximately 45 minutes in length, for 3 months at an intensity of 70-80% of maximum heart rate. The authors mentioned a significant increase in the $CD4^+$ T count and cardiorespiratory condition the experimental group.

Smith et al. [9] conducted a 12-week study (at least 30 minutes of exercises, three times per week) that assessed fatigue, dyspnea, forced expiratory volume, total body mass and body composition, $CD4^+$ T lymphocyte count and viral load outcomes in 60 patients (52 men and 8 women) randomized into 2 groups (experimental and control), all of whom were receiving HAART (7 in each group were receiving Protease Inhibitor at the beginning of the study) in a supervised aerobic training program, with the intensity monitored by the corresponding heart rate of 60-80% VO_{2max}. The control group performed their usual activities normally. It was identified a significant decrease in fatigue, total body mass and body composition of the experimental group. Cardiorespiratory condition (VO_{2max}), dyspnea, $CD4^+$ T lymphocyte count and viral load showed no significant difference in both groups.

Baigis et al. [10] studied 99 sedentary patients who were not receiving HAART. Fifty-two of these patients performed aerobic training for 15 weeks (20-minute sessions, three times per week) at 75%-85 of the estimated H_{Rmax}, and forty-seven continued with their usual treatment (control group). The study showed no significant difference in $CD4^+$ T count and in cardiorespiratory condition (VO_{2max}).

Another study from Terry et al. [11] avaliated aerobic training associated with nutritional control plus diet (experimental group) against nutritional control only (control group) for 12 weeks (36 sessions of 30 minutes, three times per week at 70%-85% H_{Rmax}) in 42 patients (26 men and 16 women who received protease inhibitors and/or non-nucleoside inhibitors of reverse transcriptase 6 months prior to the study) with dyslipidemia and lipodystrophy. VO_{2peak}, body composition, $CD4^+$ T lymphocyte count and viral load, and lipid profile were verified. There was significant improvement in the increase in VO_{2peak} of the experimental group and, in both groups, body composition considerably improved. No significant changes were found in virologic and immunologic variables.

No	Training	Author and Year	Sample Size	Variables	CD4+ T	VL
1	Aerobic	Terry et al. 1999	21 patients (14 men and 7 women)	Functional capacity Anthropometric Measurements Depression Scores CD4+ T lymphocytes Viral Load	=	=
2	Aerobic	Perna et al. 1999	21 patients (11 in the experimental group and 10 in the control group)	Cardiorespiratory Function (VO2max) CD4+ T lymphocytes n	↑	NR
3	Aerobic	Smith et al. 2001	60 patients (52 men and 8 women)	Fatigue Cardiorespiratory condition (VO2max) Dyspnea Total body mass Body composition CD4+ T lymphocyte	=	=

				Viral Load		
4	Aerobic	Baigis et al. 2002	99 patients	CD4+ T lymphocyte Cardiorespiratory condition (VO2max)	=	NR
5	Aerobic	Terry et al. 2006	42 patients (26 men and 6 women)	VO2peak Body Composition CD4+ T lymphocyte Viral Load Lipid Profile	=	=
6	Concurrent	Grinspoon et al. 2000	54 patients men	Cardiorespiratory Condition (VO2max) Muscle Mass CD4+ T lymphocyte Viral Load	=	↓
7	Concurrent	Driscoll et al. 2004	25 patients (20 men and 5 women)	Condition (VO2max) Resistance CD4+ T lymphocyte Viral Load	=	=
8	Concurrent	Fillipas et al. 2006	35 patients men	Self-efficacy Cardiovascular Condition (VO2max) Quality of life CD4+ T lymphocyte Viral Load	=	=
9	Concurrent	Dolan et al. 2006	40 patients women	Cardiovascular Condition (VO2max) Body Composition Lipid Profile Glucose Blood Pressure CD4+ T lymphocyte Viral Load	=	=
10	Concurrent	Farinatti et al. 2010	27 patients	Physical Fitness Muscular Condition CD4+ T lymphocyte	=	NR

Table 1: Summary of the outcomes described in the aerobic and concurrent training programs with multiple sets. NR (not rated)=(There was no significant difference) ↑ (significant increase); The studies presented below are organized in aerobic and concurrent training with multiple sets.

Opinion on the studies on aerobic training

In this review, only one study [8], showed an increase in the number of $CD4^+$ T lymphocytes. In other studies, there was no significant change. Similarly, no effect on plasma viremia was observed. Thus it is possible to affirm that the intensity-controlled aerobic training is a safe intervention in HIV-positive individuals,

since it does not negatively interfere in the immunologic ($CD4^+$ lymphocyte count) and virologic markers (viral load).

Concurrent training with multiple sets

Concurrent training with multiple sets was evaluated in five studies: Grinspoon et al., Driscoll et al., Fillipas et al., Dolan et al. and Farinatti et al. [12-16]. Grinspoon et al. [12] conducted a randomized controlled trial to investigate concurrent training associated with testosterone (experimental group) compared to the training and placebo (control) for 12 weeks, consisting of 20 minutes of aerobic exercise, three times a week, at 60%-70% H_{Rmax} (age-predicted), followed by progressive resistance training at 60%-80% 1RM in 54 eugonadal men on HAART with wasting syndrome. The cardiorespiratory condition was not assessed, but was found to have increased muscle mass in the experimental group. In both groups, $CD4^+$ T showed no significant increase, however, the viral load decreased significantly in the experimental group.

Driscoll et al. [13]assessed the concurrent training associated with metformin in 25 people (20 men and 5 women) receiving HAART and who completed 12 weeks of concurrent training (20-30 minutes of aerobic training at 60%-75% H_{Rmax} and three sets of 10 repetitions of resistance training at 60%-80% 1RM, three times per week). The group that underwent concurrent training associated with metformin (n=11) significantly improved cardiorespiratory condition and resistance compared to the group that only received metformin. CD4+ T lymphocyte count and viral load showed no significant inter or intragroup differences.

Fillipas et al. [14] conducted a study for the comparison of self-efficacy, cardiovascular condition, quality of life and health status ($CD4^+$ T and CV) in 35 HIV-infected men. The study was conducted for 24 weeks, while a group underwent concurrent training (20 minutes of aerobic training at 60%-75% H_{Rmax} and three sets of 10 repetitions of resistance training at 60%-80% 1 RM, twice per week) the control group was encouraged to go for walks twice a week, without supervision. There was no significant difference in any group, either in $CD4^+$ T lymphocyte count or viral load.

Dollan et al. [15] assessed VO_{2max}, strength, body composition, lipid profile, glucose, blood pressure, $TCD4^+$ T and CV outcomes in 40 HIV-infected women receiving HAART. Participants received the necessary equipment for a 16-week home-based concurrent training program (20-30 minutes of aerobic training at 60- 75% H_{Rmax} and three to four sets of 8-10 repetitions of resistance training at 60%-80% 1RM, three times per week).There was no difference in laboratory markers of HIV infection. There was a significant increase in VO_{2max}, resistance and body composition.

Farinatti et al. investigated the effects of concurrent training on physical fitness and immune function of 27 HIV-infected individuals on HAART. Eight patients were assigned to the control group and nineteen to the experimental. The experimental group underwent a 12-week concurrent training program (30 minutes of aerobic training and three sets of 12 repetitions of five types of resistance exercises at 60-80% 1RM, three times a week). Again, there were no significant differences in $CD4^+$ T lymphocyte count in the groups prior to and after the training period; however, there was an improvement in the physical fitness and muscular condition of the subjects.

Opinion on the studies on concurrent training with multiple sets

In assessing immune parameter, no concurrent training studies with multiple sets showed significant reduction or increase in $CD4^+$ T cell count. Only the study of Grinspoon et al. [12] showed a reduction when assessing the viral load in people from the experimental group who received testosterone associated with concurrent training. In summary, concurrent training with multiple sets can also be considered a safe intervention in HIV-positive patients, since it does not interfere negatively in virologic and immunologic markers.

Conclusion

From the results of this systematic review of randomized clinical trials, it is suggested that aerobic training and competing with multiple sets not interfere with the predictors of progression of HIV infection ($CD4^+$ cell count and HIV viral load). It is also suggested that they could be used as a safe non-pharmacological intervention in order to try to reduce cardiovascular risk and mitigate possible adverse events related to HAART. It should be noted that no study of isolated resistance or concurrent training with single sets the parameters of HIV results was not found.

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