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Prolonged and Shorter Aerobic Exercise Training in HIV

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Abstract

The purpose of this review was to determine whether prolonged aerobic exercise training was as safe and effective as shorter aerobic exercise training. Shorter time period studies up to and including four months were summarized for aerobic exercise training parameters and results. Similarly, aerobic exercise training studies that were six and more months were also summarized. Predicted or measured maximum oxygen uptake (VO2max) results for the shorter term studies generally ranged from 10-29%. All the studies used 3x/wk. as a training frequency. Aerobic exercise training intensity averaged 75% of predicted heart rate (PHR) maximum and exercise duration ranged from 20-60 minutes. Since many of the subjects were on highly active antiretroviral therapy (HAART), blood lipids and body fat abnormalities were prevalent. In the few shorter aerobic exercise training studies to measure lipids and body fat, there appeared to be a favorable effect. Prolonged aerobic exercise training results were sparse. Studies indicated similar training parameters with the exception of using a higher aerobic training intensity for one study. VO2max results for the higher intensity study demonstrated a higher aerobic fitness than other studies. All the prolonged aerobic exercise regimes increased VO2max similar to the shorter term studies or maintained higher levels of aerobic fitness. Triglyceride levels were elevated and unfavorably increased during prolonged aerobic training. Body fat was favorably modified in another prolonged study in spite of HAART. Considering the paucity of studies it appears that prolonged aerobic exercise training is equally safe and effective as compared to shorter aerobic exercise training.

Keywords: HIV; Aerobic exercise training; Physical activity; Physical fitness

Introduction

Various reviews have shown exercise to be safe and effective for those infected with HIV [1-4]. These reviews have examined aerobic, resistance, and flexibility exercise. The components of exercise such as intensity, duration, frequency and type have been reviewed. Yet there hasn't been an examination of the length of training. In particular aerobic exercise has not been reviewed relevant to shorter versus prolonged training results for those with HIV.

The importance of the length of training lies in the accrual of beneficial physiological effects. The primary benefit of aerobic exercise training success is an increase in maximum oxygen uptake (VO2max). An increase in VO2max increases the efficiency of the cardiopulmonary system and facilitates more work with less effort expended. Oxygenated blood is delivered more effectively and breathing frequency is reduced at a given workload. Improved VO2max through proper aerobic exercise training increases functional status, improves certain immune function indices, increases lean body weight, while decreasing adipose tissue and improves mood in those persons with HIV [5]. An elevation in cardiopulmonary work capacity or aerobic fitness has had positive and beneficial effects on body composition, overall health and quality of life [1].

HIV is a progressive, destructive immune disease, and determining whether aerobic exercise provides beneficial physical and functional changes over a longer period of time is paramount. Intuitively, if aerobic exercise provides positive physiological training effects over a shorter period one could expect this trend to continue over a longer time period. However, the pathology of HIV and the immune system destruction over time may in turn prevent or lessen the beneficial physical changes derived from prolonged aerobic exercise training. With advances and extensive use of highly active antiretroviral therapy (HAART), morbidity has improved and longevity increased [6]. However, HAART and advances in antiretroviral therapy has contributed to potentially harmful side effects. Since HAART was introduced lipid abnormalities, insulin resistance, osteopenia and increased risk of cardiac diseases have emerged [7]. Also, another reported side effect from HAART, after six months of use, has been peripheral lipodystrophy and decrease in lean body mass [8].

Since increased VO2max is critical to beneficial physiological changes for someone with HIV, this review focused on studies with the following inclusionary characteristics. Aerobic fitness or VO2max was measured either by indirect spirometry or by estimating VO2max through total treadmill time. Other inclusion criteria for study selection were, having at least one group, only performing aerobic exercise, and subjects performing aerobic exercise training having a diagnosis of HIV. Studies which had a combination of aerobic and resistive exercise performed by a subject or group were excluded secondary to possible contamination of resistive training effects on aerobic exercise.

In this review shorter term aerobic training in HIV was defined as studies from 6-16 weeks. This range of time was selected since beneficial training effects begin no sooner than 6 weeks and can take up to 16 weeks to accrue [9]. Prolonged aerobic exercise training was defined for this review as studies ranging from 24 weeks or approximately six months and longer.

This specific review will examine whether there is evidence that aerobic exercise performed regularly for at least six or more months provides beneficial physical training effects. Also, the review will seek to determine whether prolonged aerobic exercise imparts greater physiological benefits than shorter term investigations. Additionally, since aerobic exercise has been studied in those with HIV, few studies have examined whether prolonged aerobic exercise has demonstrated favorable body fat and blood lipid outcomes compared to shorter term studies.

Shorter Term Aerobic Exercise Training

There were eight studies found that fit the inclusionary criteria

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outlined previously (Table 1). Predicted or measured peak oxygen uptake of 10-29% were found [10-16] in shorter aerobic exercise training protocols. Only one aerobic exercise training study found little to no measureable change in aerobic fitness [17]. For an adult without HIV, oxygen uptake increases of at least 15%, tends to provide a greater degree of training effects [18]. Consequently, the majority of these aerobic exercise regimes of 4 months or less increased oxygen uptake to a point where beneficial physical changes resulted. Closer examination of the shorter term aerobic exercise studies reveals that an increase of aerobic fitness of less than 10% was found in aerobic exercise training of reduced session duration [17].

The average length of aerobic exercise training for the shorter term studies was approximately 12 weeks (Table 1). A "moderate" intensity was the theme and this aerobic exercise intensity was generally monitored for compliance and accuracy by pulse rate and/or rate of perceived exertion (RPE). The mode or type of aerobic exercise most often used was cycle ergometer and/or walking and/or jogging.

The subjects for these shorter duration aerobic exercise studies consisted of mostly (77%) males, between the ages of 18 and 60 years of age, and all were diagnosed with HIV and most were receiving highly active antiretroviral therapy (HAART) and/or protease inhibitors medication. HAART has a tendency to increase blood lipids and adversely alter body composition [7,8]. Consequently, these adverse changes could negatively impact oxygen uptake. As a training effect, significantly lowered body fat and/or decreased triglycerides levels were not observed in spite of a significantly increased aerobic fitness [16]. However, both triglycerides and body fat were decreased in two other investigations [14,15]. Terry et al. had dietary therapy as part of the treatment for the aerobic exercise group, although the decreases were more pronounced without a dietary component [15]. Smith et al. had lowered body fat but some of the subjects were not on HAART [13].

The clustered designation T-lymphocyte helper cells (CD4+) counts and viral loads, when reported, suggested less immunosuppression since the majority of subjects in the eight studies were around 500 cells/μL of CD4+ at the start of training. However, compliance was still a problem with some studies [11,13] having rates of approximately 60%. The subject numbers at the beginning of the shorter term studies ranged from 15 to 30. But by the end, attrition had reduced the numbers significantly [13,16]. Some of the lack of compliance and attrition was thought to be due to illness symptoms associated with HIV.

Prolonged Aerobic Exercise Training

Aerobic exercise training in HIV for approximately six or more months has been sparse. In the only investigation with a control group which did not exercise, Multimura et al. [19] had very little attrition or lack of compliance for the 50 male and female subjects with HIV. Subjects aged in range from 21-50 years. Initially the CD4+ cell count averaged approximately 350 cells/μL for all subjects. Jogging was used as the predominant type of aerobic exercise. Intensity monitoring was done by heart rate and RPE. As noted in Table 2, peak oxygen uptake-VO2max increased approximately 15% for the exercise group, but there was no change in the non-exercise group. Associated training effects with increased VO2max were decreased body fat, based on skinfold measurements. Decreased waist circumference, BMI and altered body fat redistribution were also found. Most of the subjects were on HAART which has been associated with anthropometric and metabolic abnormalities [20,21].

The next prolonged aerobic exercise training investigation was done before HAART was implemented. At the beginning of a 24 week aerobic exercise trial, 25 subjects were measured for VO2max [22]. The CD4+ cell count mean for the 25 subjects with a mean age of 35 years, was 144 cells/μL. In the two group prospective design both groups

Author(s) year	Intensity of aerobic exercise (% of max)	Duration of aerobic exercise (minutes)	Frequency of aerobic exercise (Days/wk.)	Intenvention time period (weeks)	VO2max% increase	Triglyceride change (mg/dL)	Body fat
Stringer et al. [10]	Mod. Grp.=60%; High Grp.=80% of VO2max	Mod. Grp.=60 High Grp.=40	3	6	15 in high grp.	Not measured	Not measured
Perna et al. [11]	70-80% of MHR	45	3	12	12	Not measured	Not measured
Terry et al. [12]	Mod. Grp.=60%; High Grp.=85% of MHR	30	3	12	10 in Mod. Grp; 29 in High Grp.	Not measured	Not measured
Smith et al. [13]	60-80% of VO2max	30	3	12	11 (treadmill time)	Not measured	↓
Thoni et al. [14]	Approximately 60% (HR at VT)	45	2	16	10+	237 pre; 134 post	↓
Baigis et al. [17]	75-85% of MHR	20	3	15	1	Not measured	Not measured
Terry et al. [15]	75-85% of MHR	60	3	12	25	*325 pre; 296 post	*↓
Lindegaard et al. [16]	65-75% of VO2max	40	3	16	15	No change	No change

Abbreviations: PMHR: Predicted Maximum Heart Rate; MHR: Maximum Heart Rate; HR: Heart Rate; VT: Ventilatory Threshold; VO2max: Maximum Oxygen Uptake.
*Includes dietary intervention.

Table 1: Shorter aerobic exercise training results.

Author(s) year	Intensity of aerobic exercise (% of max)	Duration of aerobic exercise (minutes)	Frequency of aerobic exercise (Days/wk.)	Intervention time period (weeks)	VO2max% increase	Triglyceride change (mg/dL)	Body fat
Multimura et al. [19]	45-75% PMHR	45-60	3	24	15	Not measured	↓
Birk et al. [24]	60-70% VO2max	40	3	52	1 (Maintained at 40-41 ml·kg^{-1}·min^{-1})	263 pre; 326 post	Not measured
Birk and MacArthur [23]	60-70% VO2max	40	3	52	1 (same as above study)	Measured in above study	Not measured
MacArthur et al. [22]	Grp. 1@75-85%; Grp. 2@50-60% (VO2max)	45	3	24	24	Not measured	Not measured

Abbreviations: see Table 1.

Table 2: Prolonged aerobic exercise training results.

used jogging, 4-limb bicycle ergometer, stair climbing and rowing as types of aerobic exercise. But the higher intensity group started with six, 4 minute intervals and the lower intensity group began with four, 10 minute intervals, for 3 times per week. As the study progressed subjects increased duration to eventually 45 continuous minutes (Table 2). Much of the significant VO2max increase was found after a 12 week submaximal measurement of aerobic fitness. The final VO2 results were obtained from six subjects. Three subjects from the higher intensity group and three from the lower intensity group. The significant attrition can be primarily explained by low CD4+ cell counts which contributed to AIDS like symptoms. These symptoms prevented at least 60% of the dropouts from exercising regularly. The six aerobic exercise compliant subjects all had higher (mean of 209 cells/μl) CD4+ cell counts at the start of the six month study.

Birk and MacArthur [23] found that after one year of regular aerobic exercise, VO2max was maintained. The six males with HIV from a previous study [23] continued aerobic exercise training for another six months (Table 2). The types of aerobic exercise used were similar to those described [22]. Five subjects finished the study. One of the subjects dropped out after month seven, secondary to AIDS symptoms illness. His CD4+ cell count had been 23 cells/μL prior to the start of the study. Another subject also experienced AIDS like symptoms and thus had erratic compliance but did finish the VO2max measurement at the conclusion of the study. However his VO2max value had decreased from 45 $ml \cdot kg^{-1} \cdot min^{-1}$ to 30 $ml \cdot kg^{-1} min^{-1}$. Also, his CD4+ cell count had gone from 242 to 21cells/μL by the end of the study. Consequently, in examining the data from the other four subjects, VO2max was maintained or slightly elevated after one year of regular, continuous aerobic exercise training. In predicting dropout besides very low CD4+ cell counts, significant body weight loss appears to have some validity. The first subject who dropped out lost approximately over 5 kg in less than two months, while the second subject who finished the study but with erratic compliance lost over 9 kg during the year long trial. Significant loss of weight especially muscle mass contributes to increased weakness and fatigue [23].

As part of the previous study [23], a separate analysis was conducted on lipids to determine whether increased aerobic fitness was a positive influence [24] (Table 2). For the five male subjects cited in the previous study [24] only triglycerides were abnormally elevated prior to the year-long aerobic exercise trial. HDL-C was also low (mid 30's mg/dL) but not significantly abnormal and fitted the inverse profile of higher triglycerides in HIV men [25]. What was abnormal was not only the triglyerides value of 263 mg/dl at the start of the study but the heavy, cloudy hypertriglyceremic appearance of the supernate. By the end of the one year study, triglycerides had further risen to over 326 mg/dL.

Conclusions

The design of some of the prolonged aerobic exercise studies makes definitive conclusions more speculative. But considering the attrition, low subject numbers, or a lack of a non-exercising control group [22-24], VO2max results were superior to all but one shorter aerobic exercise training study [15]. A prolonged aerobic exercise study [19] which did have a control group and adequate subject number entry and completion, showed VO2max increases greater than most of the shorter term aerobic exercise training studies. The Multimura et al. [19] study had subjects with higher CD4+ cell counts compared to the other prolonged aerobic exercise investigations [22-24]. CD4+Levels under 200 μl typically demonstrate lesser aerobic exercise gains secondary to greater illness days [26]. Hence, the subjects may have been healthier and not as prone to attrition and lack of compliance secondary to what the other prolonged aerobic exercise studies reported [22-24]. The higher CD4+ cell count may have been associated with HAART which was not fully implemented in the Birk and MacArthur studies [22-24].

One of the AIDS like symptoms associated with a low CD4+ cell count, and likely partially responsible for aerobic exercise attrition was a significant and sudden loss of body weight [22-24]. While body composition was not measured the sudden loss of body weight was indicative of both fat and lean masses. The significant loss and sudden loss of body weight and associated weakness appeared to be a more accurate predictor of aerobic exercise intolerance than CD4+ cell count of approximately 200 cells/μL or less.

The Multimura et al. [19] study demonstrated that adipose tissue problems associated with HAART can be lessened with prolonged aerobic exercise. A loss of body fat was also observed with shorter aerobic exercise and diet modification [15]. Body fat was decreased in shorter aerobic exercise [13], but the majority of the subjects were not on a HAART regime. Thoni et al. [14], in shorter aerobic exercise, also found body fat to diminish and showed significant decreases in triglycerides while most subjects were on HAART.

Hypertriglyceremia, prevalent with HAART, were not measured in the prolonged aerobic exercise study by Multimura et al. [19]. However, earlier prolonged aerobic exercise [24] showed that hypertriglyceride levels further increased. Since shorter aerobic exercise studies using HAART indicated that elevated triglycerides did decrease [13,14], another explanation needs consideration. All of the subjects in the shorter aerobic exercise studies which exhibited a decrease in triglycerides had higher and more moderate CD4+ levels. While the few subjects in prolonged aerobic exercise had much lower CD4+ levels. These lowered CD4+ levels and the associated loss of body weight and increased weakness may have prevented the elevated aerobic exercise kcal expenditure needed to increase lipoprotein lipase [27]. Diminished lipoprotein lipase has been postulated as a casual mechanism for elongated triglyceride clearance time in HIV [25].

Recommendations

More controlled trials with larger subject numbers are needed to accurately determine whether prolonged aerobic exercise has additional merit both in elevation of aerobic fitness and associated training effects such as reduction of blood lipids and modification of body composition. The majority of people with HIV are on HAART. While typically having higher CD4+ levels and lower viral loads, AIDS like symptoms are reduced [6]. This would enhance the compliance for prolonged aerobic exercise training investigations at higher intensities. Perhaps higher intensity aerobic exercise could alter body composition and blood lipids more favorably than what has been briefly observed in shorter aerobic exercise training.

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