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Physical activity and immunity in HIV-infected individuals

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Abstract *The purpose of this study was to determine what relationship exists among physical activity levels and viral load and CD4+ cell count in HIV-infected individuals. Increased viral load is associated with disease progression and symptom severity. A convenience sample of 66 male and female subjects between the ages of 18 and 64 years of age (mean 39 ± 8) was recruited from a hospital-based HIV/AIDS clinic. Components of PA were assessed for three continuous days using a mini-motion logger wrist actigraph. These components included mean PA level, and PA index and acceleration index. Pearson's correlational analysis was used to test the strength of association between PA components and viral load or CD4+ cell count. A significant inverse relationship was found between mean PA level and viral load ($p = 0.047$). An inverse relationship was also observed between PA index and viral load ($p = 0.0061$). Neither mean PA nor PA index scores correlated with CD4+ cell counts. Acceleration index, a measure of PA intensity, showed no correlation to viral load or CD4+ cell counts. These findings suggest that increasing levels of physical activity might have beneficial effects on viral load in HIV-infected individuals.*

Introduction

Human immunodeficiency virus-1 (HIV) infection and Acquired Immune Deficiency Syndrome (AIDS) pose serious risks to the health of millions. Despite decades of research, no cure or vaccine has been found to prevent this disease and the resultant morbidity and mortality. Regular physical activity offers many mental and physical health benefits to participants (US Department of Health and Human Services, 1996). Although regular exercise training has been shown to elicit beneficial changes in HIV/AIDS patients, it is unknown what association, if any, exists between daily physical activity and markers of disease in HIV/AIDS patients.

Physical activity is any bodily movement produced through muscular activity that results in energy expenditure. Physical fitness is defined as a set of attributes that people have or

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achieve that relates to the ability to perform physical activity. Exercise is a sub-type of physical activity that is structured and designed to improve one or more components of physical fitness. The US Surgeon General's Report recommends that all US adults complete 30 minutes of moderate intensity physical activity on most if not all days of the week. Pate *et al.* (1995) summarized the benefits of daily physical activity, stating that increasing daily physical activity will decrease the risk of chronic disease and may contribute to improved quality of life. Blair *et al.* (1989) summarized the relationship between physical fitness and all-cause mortality, stating that increased physical fitness will lead to decreased all-cause mortality. Neither physical fitness nor regular physical activity has been quantified in HIV-infected individuals or people with AIDS.

Exercise and HIV-infected individuals

Exercise interventions have been performed in both HIV-infected individuals and people with AIDS. LaPerriere *et al.* (1991, 1994) reported that aerobic conditioning increased CD4+ cell counts. Conversely, studies by Smith *et al.* (2001) and Rigsby *et al.* (1992) found that 12 weeks of aerobic conditioning and 12 weeks of combined resistance training and aerobic conditioning, respectively, had no effect on viral load or CD4 counts. Similar results were reported by Roubenoff and colleagues (1999) following eight weeks of progressive resistance training. MacArthur *et al.* (1993) have linked lower CD4+ cell count levels with non-compliance to prescribed exercise. The inconsistencies in the effects of exercise on CD4+ cell counts may stem from the different populations being examined. In those seronegative for HIV, exercise training will have little effect on CD4+ cell counts. The one group that did observe a change in CD4+ cell counts with exercise worked with a population of lower socio-economic status than did the other authors. LaPerriere and colleagues studied people with lower socio-economic status and greater life stress compared to the other authors. These authors suggest that their study used exercise as a form of stress management and the rise in CD4+ cell counts represents a normalization of stress-induced CD4+ cell depletion.

One epidemiological study examining exercise behaviours and disease status in this population was carried out by Mustafa *et al.* (1999). They found that HIV-infected individuals self-reporting exercise participation had 107.5% higher CD4+ counts when compared to HIV-infected subjects that denied exercise participation. Subjects reporting regular exercise participation also displayed slower disease progression to AIDS, less symptomology and decreased rates of mortality compared to non-exercisers. While causal relationships cannot be determined using correlational data, no similar study has been carried out examining the relationship between physical activity and disease state in this population.

Purpose

The benefits of regular exercise are well established in individuals infected with HIV. What remains unknown is the association between daily physical activity and disease markers among HIV-infected individuals. The purpose of this study was to determine what level of association exists between physical activity and CD4+ cell counts and HIV-RNA viral load in HIV-infected individuals.

Methods

Subjects

Subjects were selected from the pool of HIV-infected individuals being treated at a local hospital. Subjects were recruited with the use of flyers and through a referring medical doctor. Patients were eligible for inclusion if they were HIV-positive, 18 years of age or older, able to read and understand English at a sixth-grade level and receiving care at our referring clinic. Subjects were required to sign a medical release form giving their health care provider permission to release the results of their most recent CD4+ cell count and HIV-RNA viral load test. All laboratory results were less than 12 weeks old. A convenience sample of 66 male and female subjects (mean age = 39 ± 8 years) was utilized in this study. All subjects were on antiretroviral medications. The ethnic breakdown of the subjects was representative of the HIV-infected population of Columbia, South Carolina, with 61 African Americans (92%), three Caucasians (5%) and two Hispanics (3%). Subjects were paid \$75.00 for their participation in this study.

The Institutional Review Board at the University of South Carolina approved the study design. The mini-motion logger wrist actigraph (Ambulatory Monitoring, Inc., Ardsley, NY) was worn on the non-dominant hand of the subject for three days. During this time each subject was instructed to maintain his or her normal level of daily physical activity. Following three days of data collection the wrist actigraph was returned and all data downloaded to a computer. The wrist actigraph allows for the estimation of several physical activity component scores, including physical activity index, mean physical activity level and acceleration index. Minutes of sleep per night are also estimated. Physical activity index is calculated as the percentage of time units where activity levels were recorded at greater than zero. This value represents the percentage of time units (minutes) during the assessment period that the wrist actigraph recorded activity. Mean physical activity levels are calculated as the average minutes of physical activity performed per day over the data collection period. Acceleration index is a measure of physical activity intensity.

Physical activity measured by wrist actigraph

Wrist actigraphy has been used successfully to measure physical activity in cancer patients (Sarna & Conde, 2001), hypertensive patients (Mansoor *et al.*, 2000), elderly subjects (Shapiro & Goldstein, 1998), cardiac patients (Redeker & Wykpiusz, 1999) and apparently healthy individuals (Sugimoto *et al.*, 1997; Westerterp, 1999). Physical activity scores measured by wrist actigraph are reliable and valid. A 1993 study by Patterson *et al.* found that physical activity levels and intensities correlated significantly with oxygen uptake ($r = 0.73$) and heart rate ($r = 0.71$) both at rest and during exercise. Test-retest reliability was high ($r = 0.98$). The assessment period of three days is the standard amount of time used for physical activity measurement in classic accelerometer based physical activity assessment studies (Bell *et al.*, 1971).

Laboratory and psychological variables

CD4+ cell counts and HIV-RNA viral load were obtained from health care providers through retrospective chart review. A trained research assistant also administered several surveys. These surveys included the Pittsburgh Sleep Quality Index, Epworth Daytime Sleepiness Scale, the Piper Fatigue Scale, the State-Trait Anxiety Index and the Perceived Stress Scale.

All data were entered into SAS 8.0 for further analysis. Strength of association between variables of interest was evaluated using Pearson's correlation.

Results

The mean CD4+ cell count in our sample (412 ± 271 ; range = 8 to 1,140) indicated that the subjects were primarily in the symptomatic stage of HIV disease. Viral load ($38,571 \pm 84,437$) ranged from undetectable to 516,000 viral copies. The average minutes of physical activity recorded among our subjects was 144 ± 31 minutes per day, with values ranging from 43 minutes to 193 minutes. Low, moderate and high intensity activities are all included in this value. Physical activity index averaged $84 \pm 8.4\%$ and acceleration index averaged -0.22 .

Physical activity index as measured by wrist actigraph was inversely associated with HIV-RNA viral load ($p = 0.0061$, $r = -0.425$). The mean physical activity level over the three collection days was also negatively associated with viral load ($p = 0.047$, $r = -0.318$). Neither mean physical activity nor physical activity index scores correlated with CD4+ cell counts ($p = 0.334$ and $p = 0.126$, respectively). Acceleration index, a measure of physical activity intensity, showed no correlation to viral load ($p = 0.467$) or CD4+ cell counts ($p = 0.59$). Table 1 summarizes these findings.

Physical activity index was not associated with symptom severity ($p = 0.67$), sleep quality ($p = 0.39$), daytime sleepiness ($p = 0.608$), fatigue ($p = 0.78$), state anxiety ($p = 0.8$), trait anxiety ($p = 0.57$) and perceived stress ($p = 0.626$). Mean physical activity levels demonstrated similar relationships with symptom severity ($p = 0.76$), sleep quality ($p = 0.54$), daytime sleepiness ($p = 0.18$), fatigue ($p = 0.69$), state anxiety ($p = 0.9$), trait anxiety ($p = 0.38$) and perceived stress ($p = 0.92$).

Discussion

This study is the first to report an inverse relationship between physical activity and viral load in HIV-infected individuals. This study is also the first descriptive examination of normal daily levels of physical activity and markers of immune function in HIV/AIDS-infected individuals. Since no relationship was found between CD4+ cell counts and any physical activity component score, our results suggest that this relationship may be independent of stage of illness. Additionally, no association was observed between physical activity intensity and either viral load or CD4+ cell counts, suggesting that this relationship was not affected by physical activity intensity.

Previous studies examining the effects of exercise training in HIV-infected individuals have shown increased CD4+ cell counts (LaPerriere *et al.*, 1991; Mustaffa *et al.*, 1999). Other studies have demonstrated no effects on CD4+ cell numbers (Rigsby *et al.*, 1992; Roubenoff *et al.*, 1999; Smith *et al.*, 2001). That no relationship was found between CD4+

Table 1. Associations among physical activity variables and viral load and CD4+ cell counts

	Physical activity index	Mean physical activity	Acceleration index
HIV-RNA viral load	$r = -0.425^*$	$r = -0.318^{**}$	$r = 0.118$
CD4+ cell count	$r = 0.226$	$r = 0.091$	$r = 0.008$

* $p < 0.01$; ** $p < 0.05$.

cell counts and physical activity, but has been previously reported after exercise training, may mean that the positive change in CD4+ cell counts is intensity dependent. That is, physical activity or exercise above a certain intensity threshold will elicit a training effect, namely higher CD4+ cell counts, while activity below this threshold will not. It is possible that no relationship between CD4+ cell counts and physical activity is seen in the current study because the mean daily activity levels or the acceleration index in this sample fail to reach the intensity required to elicit a training effect.

Previous studies have reported no effects of exercise training on viral load values (Baigis *et al.*, 2002; Rigsby *et al.*, 1992; Roubenoff *et al.*, 1999; Smith *et al.*, 2001). Among people who have the same CD4+ count, those with higher viral loads tend to have more rapid disease progression than those with lower viral load test scores. These results suggest that increasing physical activity levels could lower HIV-RNA viral load levels, without the use of antiretroviral drugs, which often have severe side effects. By lowering viral load values, it may be possible to prolong the asymptomatic period of HIV disease, decreasing the incidence of opportunistic infection and delaying the initiation of treatment. This has the potential of prolonging life, decreasing HIV-associated morbidity and decreasing the cost of treatment over the course of the disease.

Acceleration index, a measure of physical activity intensity, was not associated with viral load or CD4+ cell counts. This finding is significant because many individuals with HIV have lower than normal functional capacity levels and are unable to maintain higher intensity activities (Keyser *et al.*, 2000). Although Terry *et al.* (1999) found no deleterious effects of high intensity exercise in this population, higher intensity physical activity and over training have been shown to decrease the effectiveness of the immune system in both human and animal models (Mars *et al.*, 1998; Neiman *et al.*, 1993; Peijie *et al.*, 2003; Shephard & Shek, 1994). The results of the current study imply that longer duration, lower intensity physical activity may provide health benefits while preventing deleterious effects seen with high intensity training.

Formal exercise programmes involving aerobic and resistance training provide additional benefits to individuals with HIV/AIDS over and above the benefits seen in this study, such as preservation of muscle mass and muscle strength, increased functional capacity and increased CD4+ cell counts (Roubenoff *et al.*, 1999). This study is significant in that we have found an association between daily physical activity levels and health benefits in HIV-infected individuals. This study presents evidence that those HIV-infected individuals participating in more daily physical activity will see some health benefits compared to their counterparts that participate in little daily physical activity. Encouraging people with HIV to incorporate more physical activity into their lives, such as taking the stairs rather than the lift or walking to the shops instead of driving, may provide a simple way to increase daily physical activity levels.

One limit to a descriptive, correlational design is that no causal relationship can be determined from the data. It may be that those patients with lower physical activity levels have more severe symptoms or have more accelerated disease progression, which limits their activity levels. It is also possible that those HIV-infected individuals participating in more physical activity have lower viral load levels, leading to fewer symptoms and less disability than those HIV-infected individuals participating in lower levels of physical activity. We believe that the latter is true. We found no association between symptom severity and any component of physical activity ($p=0.67$ for PA index and $p=0.76$ for mean PA level), indicating that physical activity was not affected by symptomology in this study population. We also found that physical activity was not tied to fatigue, anxiety, perceived stress or sleep quality (p values ranged from 0.39–0.8 for mean PA index and from 0.18–0.92 for mean PA levels). This suggests that physical activity levels were not limited by fatigue, anxiety, stress or lack of

adequate sleep in this population. Additional research is needed to elucidate the relationship between physical activity and immunity in HIV-infected individuals.

Conclusion

In conclusion, this study demonstrates that physical activity, independent of intensity and stage of illness, is inversely associated with HIV-RNA viral load values. Although no causal relationship can be proven with our methodologies, the data suggests that it is the people participating in more physical activity that have lower viral load levels. Several researchers have previously shown that formal exercise programmes can favourably alter CD4+ cell counts, increase functional capacity and delay mortality and morbidity in HIV-infected individuals. The current study demonstrates that regular physical activity may also be beneficial for HIV patients as well.

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