BRIEF COMMUNICATION

Exercise Improves Cardiovascular Risk Factors, Fitness, and Quality Of Life in Hiv+ Children and Adolescents: Pilot Study

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Abstract

Children and adolescents infected by HIV through mother-to-child transmission are at high risk of developing premature cardiovascular diseases due to dyslipidemia, insulin resistance and low-grade chronic inflammation. The aim of the pilot study was to verify the effect of a playful exercise program on cardiovascular, morphological, metabolic, fitness, and quality of life outcomes. A non-randomized clinical trial consisting of 24 sessions of playful aerobic and resistive exercises was applied to 10 children and adolescents living with HIV from Florianopolis, Brazil. The following variables were obtained before and after the program: fasting total cholesterol, HDL-c, LDL-c, triglycerides, glucose, C-reactive protein, blood pressure, common carotid artery intima-media thickness (CCA-IMT), flexibility, muscular endurance, aerobic fitness, anthropometry, and measured quality of life. After the intervention, a decrease in systolic blood pressure (-6.8 mmHg, 6.6%; $p = 0.019$) and CCA-IMT (-60.0 μm, 12.2%; $p = 0.002$) was observed after 24 sessions. There was an increase in upper-limb muscular endurance (+3.3 rep.min^{-1}, 63.5%; $p = 0.002$), flexibility (+5.7 cm, 26.0%; $p = 0.001$), and quality of life (+10.4 points, 27.5%; $p = 0.003$). In our sample of children and adolescents living with HIV, a short-term exercise program was associated with improvement in cardiovascular risk, fitness, and quality of life.

Keywords

Cardiovascular Diseases / physiopathology; Exercise; Physical Fitness; Life Style; Child; Adolescent; Atherosclerosis; Carotid Intima-Media Thickness.

Introduction

Exercise is a non-pharmacological treatment for adults living with human immunodeficiency virus (HIV), because it can reduce HIV-associated symptoms, cardiovascular, morphological, metabolic abnormalities and improve fitness, anxiety and depression.[1] In children and adolescents living with HIV, only one study has demonstrated the feasibility, safety and efficacy of aerobic and resistive exercises to improve muscle strength and endurance, aerobic fitness and fat free mass.[2] This is important, since fitness is reduced in several pediatric pathological conditions and might be associated with premature mortality.[3] However, no effect on lipids was observed and cardiovascular variables were not analyzed.[2]

Although the effect of exercise on the health of children and adolescents is evident, the magnitude of the effect depends on the intervention characteristics (e.g. intensity and volume of sessions) and health status at the baseline intervention (e.g. normal values of cardiovascular and lipid profiles).[4] Since the long-term exposure to HIV infection and highly-active antiretroviral therapy (HAART) are associated with dyslipidemia, insulin resistance and low-grade inflammation that increase the risk of cardiovascular diseases,[5-7] exercise could mitigate unfavorable conditions of HIV-infected children. This study reports preliminary data on the effect of a short-term playful exercise program on cardiometabolic risk factors, our primary outcome. Fitness and quality of life were also tested as our secondary outcomes.

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Methods

Study design and patient population

This was a non-randomized clinical trial that evaluated a sample of children and adolescents before and after 8 weeks of aerobic and resistive exercises, conducted in the second half of 2008 at the Rehabilitation Center in Florianopolis, Brazil. This pilot study was carried out with 10 children and adolescents infected by HIV- through mother-to-child transmission and follow at a reference hospital for the treatment of pediatric HIV infection. Before inclusion, the patients were evaluated regarding the risk of exercise. The study was approved by the Ethics Committee of the Hospital (063/2007).

Intervention

The program consisted of 24 exercise sessions, with each session lasting 90 minutes. There was a gradual increase in the duration of aerobic and muscle resistive exercises from 40 to 60 minutes (every two weeks). A 48-hour interval was used between sessions for recovery. Each session consisted of warm-up/stretching (15 min), playful aerobic and muscle-resistance activities, such as dancing, and recreational and pre-sports games (40-60 minutes), and cool-down (10 min). Playful activities appropriate for the patients' ages were selected. Most activities were organized in a circuit system to permit the session to be more dynamic. The intensity of each session was monitored with a heart rate monitor, thus permitting to determine the exercise time in the previously calculated target zone as 50-85% of the heart rate reserve.[8]

Outcomes

Fasting serum total cholesterol, triglycerides, high-density (HDL-c) and low-density (LDL-c) lipoprotein cholesterol, glucose and ultrasensitive C-reactive protein were assayed using standard procedures.[5] Blood pressure and resting heart rate were measured as previously described.[5] Intima-media thickness of the right common carotid artery (CCA-IMT) was measured using the Vivid i system (GE, Horten, Norway) with a 12.5-MHz linear transducer. The three best images of the carotid bulb segment close to the bifurcation were analyzed.[5]

Fitness was assessed by the Fitnessgram®.[9] Flexibility was evaluated by the sit-and-reach test. Muscular endurance was assessed by the abdominal curl-up test and flexed arm hang test. Aerobic fitness was measured in a submaximal exercise test performed on a treadmill and the peak oxygen consumption was estimated.[10] Anthropometric measurements were performed using standard procedures.[11] Body mass index, trunk-extremity skinfold ratio, and upper arm muscle area were calculated. Quality of life was evaluated using the "*Autoquestionnaire Qualité de vie Enfant Imagé*".[12]

Statistical analysis

The Shapiro-Wilk test was used to verify Gaussian distribution. Descriptive analyses were presented as mean and standard deviation for data before and after the intervention. The after – before intervention differences (Δ°) were calculated to describe effects. Paired Student t-test and Mann–Whitney U test were performed, adopting a p-value ≤ 0.05 in two-tailed analyses. Statistical analyses were performed using the STATA 11.0 (Stata Corporation, College Station, TX, USA) and GraphPad Prism 5.0 (GraphPad Software, Inc., San Diego, CA, USA) packages.

Results

The sample included nine girls and one boy aged 13.0 years (interquartile range [IQR]= 11.5 to 15.5 years); 4/10 participants were white and 6/10 were in moderate to severe stages of HIV infection. Half the participants used protease inhibitors, 8/10 used nucleoside reverse transcriptase inhibitors (NRTIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs), and 2/10 were undergoing HAART. The median CD4+ T-lymphocyte count was 722.0 cells.ml^{-1} (IQR= 647.5 and 914.2) and the median viral load was 17,750 copies.ml^{-1} (IQR= 368 and 26.000). Eight of the 10 subjects were pubertal, one was prepubertal, and the other was post-pubertal. Figure 1 shows the time spent in the target heart rate zone (50-85%) during each session.

Table 1 shows the changes in outcomes after the exercise program. A decrease was observed in systolic blood pressure (6.6%) and CCA-IMT (12.2%), as well as an increase in muscular endurance (63.5%), flexibility (26.0%) and quality of life (27.5%). The CD4+ T-lymphocyte count and viral load remained unchanged after the intervention. No dropout from the exercise program or intercurrence during the program was observed.

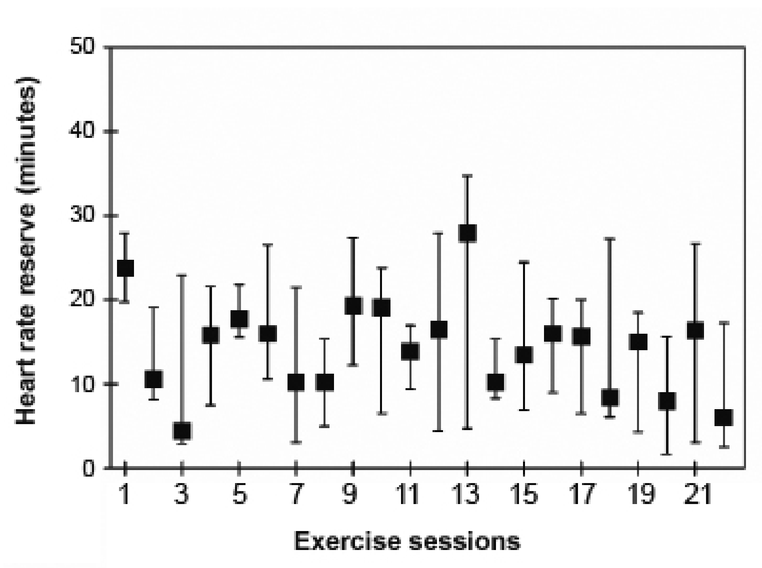

Figure 1 – *Median time in the target heart rate zone during the exercise sessions.*

Discussion

This study demonstrated a positive effect of 24 sessions of a playful exercise program on systolic blood pressure, CCA-IMT, upper limb muscular endurance, flexibility, and quality of life in children and adolescents living with HIV. To the best of our knowledge, this is the first study demonstrating changes in endothelial structure after an exercise intervention program. Although preliminary, these results highlight the importance of exercise as a non-pharmacological therapy for children and adolescents living with HIV.

CCA-IMT is a surrogate endpoint measure of atherosclerosis and has been shown to be increased in several studies on pediatric HIV. [5-7] Increased CCA-IMT has been associated with elevated high blood pressure and C-reactive protein,[7] insulin and glycosylated hemoglobin levels,[6] severe symptoms of HIV infection and use of protease inhibitors,[13] long-term exposure to HAART,[14-16] increased suprailiac skinfold, stavudine use, and low CD4+ T-lymphocyte count.[5,15,17] Although we found no changes in traditional cardiovascular risk factors after the intervention, except for a reduction in systolic blood pressure, the decrease in CCA-IMT suggests regression of atherosclerotic plaque formation. Prospective observational studies have demonstrated an association between reduced carotid and aortic IMT and increased leisure physical activity[18] and aerobic fitness,[19] respectively, in healthy Finnish adolescents. Our data corroborate the findings of an intervention study involving obese children, in which a reduction in CCA-IMT was observed after 12 weeks of exercise, even in the absence of significant changes in C-reactive protein or triglyceride levels.[20]

The reduction in CCA-IMT after exercise may be explained by hemodynamic, antioxidant and antiatherogenic mechanisms (e.g., altered physical strength, upregulation of vascular eNOS and superoxide dismutase expression, downregulation of P-selectin, V-CAM and MCP-1 expression), as most of these changes occur after 4 weeks of training.[21] Likewise, we hypothesize that regression of IMT occurred rapidly due to the plasticity of the cardiovascular tissue during the pubertal period, to hypoactivity as seen in chronic diseases,[3] or to a "less favorable scenario" such as pediatric HIV infection. Moreover, the decrease in systolic blood pressure observed in our sample represents the attenuation of a cardiovascular risk factor associated with CCA-IMT.[18] We observed a decrease of 13% of HDL-cholesterol; however, the time of observation in the study was very short to verify a benefit from exercise.

Table 1 – Cardiometabolic, fitness and quality of life outcomes in children and adolescents living with HIV submitted to the exercise program (n = 10)

Outcomes	Pre- Intervention	Post- Intervention	Δ°	p value
	Mean (standard deviation)			
Morphological				
Weight (kg)	43.8 (12.9)	44.3 (12.8)	+0.5	0.070 [a]
BMI (kg.est^{-2})	18.9 (3.2)	19.0 (3.2)	+0.1	0.267 [a]
Tricipital SF (mm)	11.6 (4.7)	12.2 (5.6)	+0.7	0.142 [a]
Subscapular SF (mm)	11.2 (10.6)	11.3 (10.3)	+0.1	0.918 [b]
Bicipital SF (mm)	4.8 (2.4)	5.5 (3.5)	+0.7	0.307 [a]
Suprailiac SF (mm)	20.8 (12.3)	20.9 (11.3)	+0.9	0.933 [a]
ΣSF (mm)	48.4 (26.4)	50.0 (27.3)	+1.6	0.292 [a]
Abdominal circumference (cm)	62.0 (21.4)	68.2 (9.9)	+6.2	0.878 [b]
TER (s/u)	1.84 (0.7)	1.78 (0.7)	-0.06	0.646 [b]
UAMA (cm^2)	28.3 (9.4)	28.2 (8.0)	-0.1	0.910 [a]
Metabolic and inflammatory				
Total cholesterol (mg.dL^{-1})	164.1 (22.1)	162.3 (28.8)	-1.8	0.822 [a]
Triglycerides (mg.dL^{-1})	137.3 (46.7)	141.5 (45.3)	+4.2	0.641 [a]
HDL-c (mg.dL^{-1})	53.6 (9.3)	46.6 (9.7)	-7.0	0.019 [a]
LDL-c (mg.dL^{-1})	83.0 (13.7)	87.6 (22.8)	+4.6	0.445 [a]
VLDL (mg.dL^{-1})	27.5 (9.3)	28.3 (9.0)	+0.8	0.641 [a]
Glucose (mg.dL^{-1})	80.4 (8.5)	83.9 (8.9)	+3.5	0.260 [b]
C-reactive protein (mg.L^{-1})	3.5 (6.9)	2.7 (3.2)	-0.8	0.444 [b]
Cardiovascular				
Systolic BP (mmHg)	102.6 (10.8)	95.8 (10.8)	-6.8	0.002 [b]
Diastolic BP (mmHg)	62.2 (8.9)	58.8 (6.7)	-3.4	0.120 [a]
HRresting (bpm)	77.2 (15.1)	72.1 (19.6)	-5.1	0.427 [a]
CCA-IMT (μm)	493.2 (20.8)	432.3 (60.5)	-60.0	0.005 [b]
Fitness				
MEupper limbs (rep.min^{-1})	5.2 (3.4)	8.5 (3.6)	+3.3	0.002 [a]
MEabdomen (rep.min^{-1})	21.4 (10.8)	25.8 (9.6)	+4.4	0.137 [a]
Flexibility (cm)	21.9 (9.8)	27.6 (11.7)	+5.7	0.001 [a]
Estimated VO2 peak (ml.kg^{-1}.min^{-1})	41.9 (11.3)	41.2 (12.5)	+0.3	0.508 [b]
Quality of Life				
Quality of life score (score)	37.80 (14.2)	48.20 (11.4)	+10.4	0.003 [a]

BMI: body mass index; SF: skinfold; TER: trunk-extremity ratio; UAMA: upper arm muscle area; HDL-c: high-density lipoprotein cholesterol; LDL-c: low-density lipoprotein cholesterol; VLDL: very-low-density lipoprotein cholesterol; BP: blood pressure; HR: heart rate; CCA-IMT: common carotid artery intima-media thickness; ME: muscular endurance; VO_2 peak: peak oxygen consumption. [a] paired Student's T test; [b] Mann Whitney U test.

Satisfactory levels of muscular endurance and flexibility are important because they reflect the functional capacity of the organism. In contrast, low levels of fitness may restrict the participation in sports and daily physical activities, as a result of real or perceived limitations and are even predictive of morbidity and mortality.[3] Thus, the pathological state may cause hypoactivity, which reduces fitness and functional capacity, leading to further hypoactivity.[3] In agreement with Miller et al.,[2] our data showed that exercises are effective in increasing the levels of upper limb muscular endurance and flexibility of the lumbar spine and hamstring muscles. In the context of pediatric HIV, there is a need for interventions designed to improve fitness due to poor aerobic capacity,[22,23] flexibility,[23] anaerobic power,[24] agility and lower limb strength.[23]

Exercise interventions can also improve quality of life in HIV-infected individuals. This was evidenced in our study and corroborates other investigations involving adults living with HIV.[1] Interventions should include playful and fun activities and satisfy the priorities of childhood and adolescence. For example, children need to focus on the development of motor skills, while adolescents can explore health, fitness, and physical activity behavioral components.

Conclusions

Based on our preliminarily data, we conclude that 24 sessions of aerobic and resistive exercises were successful to reduce blood pressure and CCA-IMT and to improve muscular endurance, flexibility and quality of life in children and adolescents living with HIV. Subsequent studies with larger samples using long-term interventions are necessary to support our findings and could also explore the effects of exercise on metabolic and inflammatory biomarkers.

Author contributions

Conception and design of the research: Back IC, Beck CC; Acquisition of data: Lima LRA, Back IC, Beck CC; Analysis and interpretation of the data: Lima LRA, Caramelli B; Statistical analysis: Lima LRA; Writing of the manuscript: Lima LRA, Back IC, Caramelli B; Critical revision of the manuscript for intellectual contente: Lima LRA, Back IC, Beck CC, Caramelli B.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any thesis or dissertation work.

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