Effect of an Exercise Program, on Hemodynamic, Metabolic and Inflammatory Markers in Obese Mexican Adolescents

Benigno Linares-Segovia1,2*, Juan Manuel Guizar-Mendoza3, Norma Amador-Licona4, Gloria Barbosa-Sabanero1 and Juan Manuel Malacara1

1Department of Medicine and Nutrition, Division of Health Sciences, Campus Leon, University of Guanajuato, Guanajuato, Mexico
2PEMEX Regional Hospital Salamanca, Salamanca, Guanajuato, Mexico
3University de LaSalle, Department of Research, Leon, Mexico
4Instituto Mexicano del Seguro Social, UMAE 1, Leon, Mexico

Abstract

Background: Obesity prevalence has increased in Mexican adolescents. This disease is associated with a chronic inflammatory response, which has been proposed to have an important role in cardiovascular disease. The aim of this study was to evaluate the short term effect of a moderate-intensity physical activity program on hemodynamic, metabolic, and inflammatory markers in obese adolescents.

Findings: We performed a longitudinal study in 43 healthy obese adolescents (26 female and 17 male). The study was conducted at the Mexican Institute of Social Security in Leon, Mexico. Subjects were submitted to aerobic exercise training during 90 minutes for 16 weeks, 5 days per week. Before and after the intervention program, hemodynamic, metabolic and inflammatory parameters were measured. Body weight was reduced by 4%. Blood pressure, insulin, insulin resistance, C reactive protein, interleukine 6, intracellular adhesion molecule-1 and vascular cell adhesion molecule-1 serum levels significantly decreased independently of gender while adiponectin levels increased. In the multiple regression analysis, the increase in adiponectin levels and the decrease in body mass index were related to systolic blood pressure levels (R2= 0.26; p=0.001), while final maximum O2 consumption rate and final systolic blood pressure levels were related to decrease in C reactive protein levels (R2= 0.79; p=0.0001).

Conclusions: A moderate-intensive exercise for 90 minutes a day at short term significantly diminished adiposity, hemodynamic, metabolic, and inflammatory markers in obese adolescents.

Keywords: Physical activity; Body fat; Cytokines; Adhesion molecules

Abbreviations: BMI: Body Mass Index; CRP: C Reactive Protein; (ICAM)-1: Intercellular Adhesion Molecule-1; (IL1): Interleukine 1; (IL6): Interleukine 6; (METS): Metabolic Equivalents; (TNFa): Tumor Necrosis Factor-alpha; (VCAM)-1: Vascular Cell Adhesion Molecule

Introduction

Obesity is a prevalent metabolic disorder in large parts of the developing world. In 2004, the age adjusted rates of obesity and overweight reported in the third National Health and Examination Survey (NHANES III) was 16.0% for children [1]. In Mexico, the National Health and Nutrition Survey 2006 showed a 23.3% and 9.2% for overweight and obesity prevalence respectively in 12-19 years old [2]. This represents a relative increase of 7.8% and 33.3% in overweight and obesity respectively when compared with the National Nutrition Survey 1999 [3]. Obesity is associated with a chronic inflammatory response [4], which has been proposed to have an important role in cardiovascular disease. Furthermore, the Hispanics are one of the populations that are especially prone to develop obesity and metabolic complications [5].

A recent study found that controlled aerobic exercise program, without weight loss, reduced hepatic and visceral fat accumulation, and decreased insulin resistance in obese adolescents [6]. However, there is scarce information evaluating the short term effect of a moderate intensity physical activity program on hemodynamic, metabolic and proinflammatory markers in obese Mexican adolescents.

Materials and Methods

We performed a longitudinal study in 43 asymptomatic volunteers (26 female and 17 male) obese adolescents (BMI ≥ 95th percentile according to the growth charts from the Centers for Disease Control and Prevention [7]). The sample size was estimated before the study. Forty adolescents would achieve an 80% power to detect a relative 25% decrease in C reactive protein (CRP) levels after the exercise maneuver considering a mean and standard deviation of 6.0 ± 2.5 mg/L according to a α level of 0.05 using a simple-sided t-test [8].

Adolescents were recruited on the basis of age (12-15 years) from a public high-school. All of them were healthy non-smokers, without chronic illnesses, and none had participated in athletics or regular exercise before this study. The local ethical committee approved the study, and informed consent was obtained from all participants and at least one parent.

All subjects were submitted to aerobic exercise training during 90 minutes for 16 weeks, 5 days per week according to the European Youth Heart Study recommendations [9]. The exercise program used in this study was specifically designed by investigators (L.B. and G.J.), and it consisted of the following: 1) Warm up (10 minutes): Sports-specific callisthenics such as push-ups and sit-ups; 2) Moderate effort (30 minutes): The participants performed competition skills, including take-downs, escapes, running etc.; 3) Recreational activities

*Corresponding author: Benigno Linares-Segovia, Department of Medicine and Nutrition, University of Guanajuato, Guanajuato, Mexico; Tel: +52 477 7145859 ext. 4627; E-mail: blinares70@yahoo.com.mx

Received February 08, 2013; Accepted February 25, 2013; Published February 28, 2013

Citation: Linares-Segovia B, Guizar-Mendoza JM, Amador-Licona N, Barbosa-Sabanero G, Malacara JM (2013) Effect of an Exercise Program, on Hemodynamic, Metabolic and Inflammatory Markers in Obese Mexican Adolescents. Endocrinol Metab Synd 2013, S2: 003. doi:10.4172/2161-1017.S2-003

Copyright: © 2013 Linares-Segovia B, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.
Physical activity was assessed by the International Physical Activity Questionnaire [10]. It is expressed as metabolic equivalents (METs) which represent the ratio of the energy expended during a specific activity to the resting metabolic rate. METs were assigned to each physical activity according to the Compendium of Physical Activities [11], as values of 2.5, 4.0, and 6.0 for low, moderate, and intense activity respectively. Overall fitness was assessed according to the 12-min walk-run test (12mWRt) [12], to estimate the maximal oxygen intake (VO2max).

After 10 days of exercise according to the initial physical fitness assessment, all obese children were capable to perform a 90 min training session at 60-70% of maximal heart rate. Participation in the exercise training program averaged 88.4% of scheduled visits. Blood pressure was evaluated using a mercury sphygmomanometer with a cuff covering two thirds of the right arm. After 15 minutes in rest, two readings were made within a 5 minutes interval, and the average was registered. Body fat was measured by using a body fat analyzer (TANITA model BF682).

All adolescents were instructed to go on a weight-reduction diet by a standard appointment at the nutrition department. Dietary assessment was carried out by one experienced qualified dietitian to minimize inter-individual bias among different professionals. Food quantities were estimated using Nutrikal a nutritional software package developed by Ogali (Mexico, D.F.) Venous blood was obtained after overnight fasting to determine lipid profile, glucose, insulin, leptin, adiponectin, interleukine-1 (IL1), IL6, TNFα, CRP, ICAM-1, and vascular cell adhesion molecule-1 (VCAM-1) levels. All measurements were performed at baseline and after the intervention program.

Blood glucose concentration was measured using the glucose oxidase method (Ortho Clinical Diagnostics; Johnson-Johnson). The intra-assay coefficient of variation (CV), and inter-assay CV were 1.9% and 7.5% respectively.

Serum insulin was measured with a solid phase radioimmunoassay (Diagnostic Products Corporation, Los Angeles, CA). The intra-assay CV was 5.2%, the inter-assay CV was 7.3%, and the sensitivity limit was 1.2 µIU/mL.

Serum leptin was measured by immunoradiometric assay (Diagnostic Systems Laboratories, Inc., Webster, Texas). The intra assay CV was 3.7%, the inter assay CV was 5.2%, and the sensitivity limit was 0.10 ng/mL.

Adiponectin levels were measured by radioimmunoassay (Linco Research, St. Charles, MO). The intra assay CV was 3.8%, the inter assay CV was 8.4%, and the sensitivity limit was 1.0 ng/mL.

IL1, IL6, PCR TNFa, VCAM-1, and ICAM-1 levels were measured by ELISA (Biosource International, California, USA).

Statistical Considerations

Results are expressed as mean ± SD or as median (95% CI) according to variables distribution. Differences between genders were assessed by χ2 for proportions. The Mann-Whitney U test or Student’s t-test were used for continuous variables displaying non-normal or normal distribution respectively. For comparison of continuous variables before and after the exercise program we performed ANOVA test and Tukey honest significant difference as post-hoc test. In addition, we performed ANCOVA test considering gender as covariable. Considering that systemic blood pressure has been a better predictor risk of cardiovascular events than diastolic blood pressure levels [13], and that CRP levels have been considered as a useful inflammatory marker in clinical practice [14]; forward stepwise multiple regression analysis was used to study the clinic and biochemical predictors of change in these variables. We considered F value to enter and F value to remove set to p<0.05 and p<0.10, respectively. All data were analyzed using the STATISTICS software version 6.0 (Statsoft Inc. Tulsa OK).

Results

We included 43 adolescents, 5(11.6%) withdrew the study during the first month of follow-up. At baseline, female adolescents showed lower physical activity and VO2max while BMI, diastolic blood pressure, and leptin levels were higher than male adolescents (Table 1).

Median total energy intake significantly decreased after the intervention program (2077 ± 562 vs. 1639 ± 535 Kcal; p=0.03) without difference in macronutrients distribution (51.8 ± 18.7% of carbohydrates, 14.0 ± 6.5% of proteins, and 31.0 ± 13.1% of fat) by gender or by the effect of the intervention program.

Following the program physical activity, run distance in 12 minutes and VO2max significantly increased, while body weight only reduced 4%. BMI, body fat and blood pressure levels also decreased in all the group after the intervention program, and the statistical significance persisted independently of gender (Table 2).

Glucose, triglycerides, VLDL-cholesterol, insulin, insulin resistance, CRP, IL-1, IL-6, ICAM-1, and VCAM-1 serum levels also significantly decreased after the intervention program; however, considering that systolic blood pressure has been a better predictor risk of cardiovascular events than diastolic blood pressure levels [13], and that CRP levels have been considered as a useful inflammatory marker in clinical practice [14]; forward stepwise multiple regression analysis was used to study the clinic and biochemical predictors of change in these variables.
glucose and IL-1 levels lost significance after adjusting for gender. An increase in adiponectin and LDL-cholesterol levels was observed but LDL-cholesterol levels were dependent of gender (Table 3).

Eight (21.0%) adolescents did not show weight reduction during the program; however physical activity and VO2max change, as well as hemodynamic and inflammatory markers were similar with the rest of the group (data not showed).

In the multiple regression analysis, we found that change in adiponectin levels and BMI were related to change in SBP levels (Table 4).

Final VO2max (r = 63; p = 0.004), change in BMI (r = 0.51; p = 0.06), change in BF(r = 0.72; p = 0.003), and final SBP (r = 0.47; p = 0.07) were related to decrease in CRP levels. In the multiple regression analysis, only final VO2max (β=0.63; p=0.0008) and final SBP levels (β=0.54; P=0.002) persisted in the model (R²= 0.79; p=0.0001).

All the results of the multiple regression analysis were independent of change in energy intake evaluated by 24-h recall method.

Discussion

Hispanic adolescents seems to have a high risk of being obese [15], and considering that it is necessary to reduce the risk of cardiovascular disease in childhood, we report the effect of physical training program on hemodynamic, metabolic and inflammatory markers in obese adolescents. In our study, adiposity decreased in both genders and change in BMI was significantly related to diminish in systolic blood pressure. This can be explained by changes in hormonal production according to adipocytes size. Growth of adipose tissue mass involves both hypertrophia and hyperplasia of adipocytes. Fat cell size has been related to different adipokine production of adipose tissue. Long-term-steady state weight reduction in obese subjects resulted in marked decreases in fat cell volume, leptin secretion, and serum leptin concentrations compared with control subjects, despite similar percent body fat [16]. Furthermore, exercise reduces adipocyte hypertrophy and up-regulation of PPAR(gamma) in rats with metabolic syndrome [17], which could explain at least in part the reduction in inflammatory markers, leptin, and the increase in adiponectin levels in our study.

The decrease in ICAM-1 levels after the intervention program independently of gender is a relevant end point. ICAM-1 determine a variety of lymphocyte functions but, perhaps more importantly in the context of cardiovascular disease, it also plays a pivotal role in the "trafficking" of leucocytes through tissues, interacting with beta2 integrins on white cells [18]. Even more, increased amounts of soluble ICAM-1 and E-selectin have been found in patients with atherosclerosis [19].

Adiponectin levels were negatively associated with SBP levels in multiple regression analysis, this supports the hypothesis that adiponectin reduces the inflammation status of vasculature, and in turn blood pressure levels [20]. It has been reported that adiponectin dose dependently produces inhibition of the expression of adhesion molecules VCAM-1, ICAM-1 and E-selectin, reducing monocyte’s phagocytic activity and decreasing the accumulation of modified lipoproteins in the vascular wall [21]. Weight loss is a potent inducer of adiponectin levels; however they are affected by many other factors including gender, age, and lifestyle [22]. So, the increase in physical activity even in those children without weight loss during follow up could explain the increase in adiponectin levels.

Other inflammatory and metabolic markers also improved after the intervention program. According with our results, Zicardi et al. [23], in obese women found reductions in IL6, VCAM-1 and ICAM-1 following weight loss of 10 kg; however, we demonstrated reductions in these and other parameters after only a 3.2 kg of weight reduction, and results in the multiple regression analysis were independent of change in energy intake.

Evidence exists that leptin levels are reduced in physical active individuals independent of BMI [24], and that leptin in associated with CRP levels [25]. Consequently, physical activity could decrease IL-6 and TNF-alpha levels and, ultimately, CRP production, by reducing obesity and leptin and increasing adiponectin and insulin sensitivity [26]. Even more, some of these effects may be mediated by modification of cytokine production from other sites, besides adipose tissue, such as skeletal muscles.

How exercise training reduces inflammation and suppresses markers of inflammation is not well defined. Dufaux et al. detected that the difference in CRP concentrations depended on the type of sports performed, and the proportion of aerobic endurance activities seems to be related to the degree of CRP reduction [27]. Milani et al. analyzed 12 the effects of a phase II cardiac rehabilitation program on plasma levels of hs-CRP; they reported a significant 36% reduction after the 3-month intervention independently of weight reduction [28]. This finding implies that adipose tissue is not the only source of proinflammatory cytokines.

Obesity and sedentary physical activity are important cardiovascular risk factors [29]. The American Heart Association concluded that primary prevention is the key to decreasing obesity and limiting its societal impact, particularly since the prevalence of obesity is increasing in children and adolescents [30]. In our study, all obese adolescents showed low physical activity and VO2max levels according to charts for Spanish children [29]. However, they improved their

---

### Table 3: Biochemical variables before and after physical training program in obese adolescents.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline n=38</th>
<th>After exercise n=38</th>
<th>p</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mmol/L)</td>
<td>5.1 ± 0.5</td>
<td>5.1 ± 0.5</td>
<td>0.02</td>
<td>0.08</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>4.0 ± 1.4</td>
<td>2.6 ± 1.0</td>
<td>&lt;0.0001</td>
<td>0.001</td>
</tr>
<tr>
<td>Total-Chol (mmol/L)</td>
<td>3.9 ± 0.6</td>
<td>3.9 ± 0.7</td>
<td>0.38</td>
<td>0.39</td>
</tr>
<tr>
<td>HDL-Chol (mmol/L)</td>
<td>0.9 ± 0.2</td>
<td>0.9 ± 0.2</td>
<td>0.47</td>
<td>0.49</td>
</tr>
<tr>
<td>LDL-Chol (mmol/L)</td>
<td>2.1 ± 0.5</td>
<td>2.3 ± 0.6</td>
<td>0.002</td>
<td>0.07</td>
</tr>
<tr>
<td>VLDL-Chol (mmol/L)</td>
<td>0.8 ± 0.2</td>
<td>0.5 ± 0.2</td>
<td>&lt;0.0001</td>
<td>0.001</td>
</tr>
<tr>
<td>Insulin (pmol/L)</td>
<td>21.5 (17.9 - 27.9)</td>
<td>12.9 (17.8 - 17.2)</td>
<td>0.001</td>
<td>0.01</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>0.65 (0.51 - 0.92)</td>
<td>0.38 (0.24 - 0.59)</td>
<td>0.002</td>
<td>0.02</td>
</tr>
<tr>
<td>Leptin (ng/mL)</td>
<td>21.0 (18.2 - 22.8)</td>
<td>16.5 (12.9 - 20.1)</td>
<td>&lt;0.0001</td>
<td>0.003</td>
</tr>
<tr>
<td>Adiponectin (ng/mL)</td>
<td>10.5 (4.7 - 13.5)</td>
<td>19.0 (12.9 - 32.7)</td>
<td>&lt;0.0001</td>
<td>0.0006</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>7.4 (3.1 - 10.1)</td>
<td>3.3 (2.4 - 4.4)</td>
<td>0.009</td>
<td>0.01</td>
</tr>
<tr>
<td>TNFα (pg/mL)</td>
<td>6.8 (5.7 - 11.0)</td>
<td>5.1 (4.2 - 5.9)</td>
<td>&lt;0.0001</td>
<td>0.005</td>
</tr>
<tr>
<td>IL-1 (mg/mL)</td>
<td>0.07 (0.03 - 0.09)</td>
<td>0.05 (0.03 - 0.05)</td>
<td>0.004</td>
<td>0.05</td>
</tr>
<tr>
<td>IL-6 (pg/mL)</td>
<td>3.0 (2.2 - 3.4)</td>
<td>1.5 (1.1 - 1.8)</td>
<td>&lt;0.0001</td>
<td>0.0007</td>
</tr>
<tr>
<td>ICAM-1 (mg/mL)</td>
<td>598.7 ± 115.7</td>
<td>452.4 ± 130.0</td>
<td>&lt;0.0001 &lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>VCAM-1 (mg/mL)</td>
<td>2728 (1919 - 3044)</td>
<td>1482 (1143 - 1924)</td>
<td>0.0001</td>
<td>0.005</td>
</tr>
</tbody>
</table>

*p value adjusted for gender

### Table 4: Multiple regression analysis for factors associated to change in SBP levels.

<table>
<thead>
<tr>
<th>Variable</th>
<th>β</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in adiponectin levels</td>
<td>-0.45</td>
<td>0.0002</td>
</tr>
<tr>
<td>Change in BMI</td>
<td>-0.30</td>
<td>0.04</td>
</tr>
</tbody>
</table>

R² = 0.26, intercept -8.07; Standard Error 2.68; p = 0.001 for the model
exercise capacity and aerobic energy metabolism, which have been associated with reduction in local inflammatory activation.

The main strengths of this study were the high performance of a training program, according to the proposed by the European Youth Heart Study [9], and the evaluation of hemodynamic, metabolic, anthropometric and inflammatory markers together, considering that clustering of cardiovascular disease risk factors has recently proved a better measure of cardiovascular health in children than single risk factors [31]. However a limitation of this study is the small sample size and that we did not have control group.

In conclusion, a 16 weeks programme involving 90 minutes of aerobic exercise 5 days per week significantly diminished adiposity, hemodynamic, metabolic, and inflammatory markers in Hispanic obese adolescents who are specially prone to develop metabolic and hemodynamic complications.

Acknowledgments and Funding

This study was supported by FOFOI and CONCYTEG grants (IMSS FP-2005/116 and GTO-2005-18792) respectively.

References