Interdisciplinary Therapy Improves Biomarkers Profile and Lung Function in Asthmatic Obese Adolescents

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Summary. Background: The simultaneous rise in the prevalence of asthma and obesity in the world, have demonstrated the importance of the development of treatment strategies. The purpose of this study was to evaluate the short- and long-term results of interdisciplinary therapy on inflammatory biomarkers and lung function in asthmatics obese adolescents. Methods: Seventy-six post-pubertal obese adolescents were recruited, including 50 non-asthmatics [body mass index (BMI), 36 ± 5 kg/m²] and 26 asthmatics (BMI, 39 ± 4 kg/m²). Body composition was measured by plethysmography, and visceral fat was analyzed by ultrasound. Serum levels of adiponectin, leptin, and C-reactive protein (CRP) were analyzed. Asthma and lung function were evaluated according to the American Thoracic Society criteria. Patients were submitted to 1-year weight loss interdisciplinary intervention consisting of medical, nutritional, exercise, and psychological therapy. Results: After interdisciplinary intervention, the lung function and pro/anti-inflammatory adipokines improved significantly in both groups. Most importantly, there was an increase in adiponectin [4 (1.86–12.9) to 5.1 (2.48–16)], a reduction in CRP [2,073 (385–9,174) to 1,538 (205–7,083)] and leptin concentrations [59 (29–69) to 33 (9–49)] in the asthmatics patients. Furthermore, it was observed a reduction in asthma severity after treatment. In addition, Δ adiponectin was an independent factor to improve lung function after therapy in both groups. Conclusions: Interdisciplinary therapy resulted in beneficial changes in inflammatory biomarkers profile and lung function in asthmatic and non-asthmatic obese adolescents. Additionally, for the first time we showed that change in adiponectin level was an independent predictor to improve lung function in Brazilian obese adolescents. Pediatr Pulmonol. 2012; 47:8–17. © 2011 Wiley Periodicals, Inc.

Key words: obesity; asthma; adipokine; adolescence; therapy.

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Statement of competing interests: All authors declare that the answer to the questions on your competing interest form are all No and therefore have nothing to declare.

Ethical approval: Project approval was obtained from Human Research Ethics Committee of Universidade Federal de São Paulo—UNIFESP (0135/04).

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INTRODUCTION

The prevalence of asthma and obesity has increased substantially during the last decades in many countries. Asthma is a chronic inflammatory disease of airways related to great economic burden to Brazilian Unified Health System (SUS) and to society, as well. According to DATASUS (Public Health Data Base of Brazil), in 2004, public costs with asthma were higher than 106 millions of reais. These data demonstrate the importance in the development of treatment strategies to reduce the asthma severity and costs-related.

The reasons for the relationship between asthma and obesity are uncertain. Suggested mechanisms include sedentary lifestyle, dietary factors, reduced chest wall compliance from obesity, insulin resistance, co-morbidities, and a common genetic predisposition. Other possible mechanisms include a systemic inflammatory state associated with obesity.

The inflammatory process in the lungs is characterized by the production of histamine, bradykinin, leukotrienes, and a diversity of chemokines and cytokines by tissues and migrating cells. The increase in C-reactive protein (CRP) levels in obesity may upregulate inflammation in the airway. CRP is a major inflammation-sensitive plasma protein in humans. Its synthesis by the liver is regulated to a large extent by the proinflammatory cytokine IL-6. In a recent study, mean forced expiratory volume in 1 sec (FEV1) was lower in subjects with high CRP levels, and bronchial hyperresponsiveness was more frequent.

Some studies have suggested a role of leptin in the presence of obesity associated with asthma. In previous investigation, the leptin was a predictor factor to asthma in children. Furthermore, the high concentrations of leptin are associated with impaired lung function in obese. Serum concentrations of leptin, an energy-regulation hormone, are increased in obese. This adipokine exerts an important function in the regulation of the inflammatory process. In this sense, prior investigation showed that leptin levels were increased in allergic reaction in the airways.

On the other hand, studies demonstrated that proinflammatory factors suppress adiponectin production by adipocytes. Thus, an inverse correlation between adiponectin and classic markers of inflammation has been observed in obese and insulin-resistant subjects. In addition, several reports have demonstrated the anti-inflammatory activities of adiponectin that exerts a variety of effects, ranging from inhibition of proinflammatory cytokine production to induction of anti-inflammatory factors, such as IL-10. In this sense, previous research found that adiponectin concentration was reduced during airway inflammation and hyperresponsiveness. Unfortunately, plasma adiponectin levels are decreased with obesity, although the levels increase after weight loss. However, no study has evaluated the effects of interdisciplinary therapy on biomarkers profile in asthmatic obese patients.

Thus, we hypothesized that after treatment the asthmatic patients will improve their lung function, asthma severity, and the profile of obesity-related biomarkers. Thus, the aim of the current investigation was to evaluate the effects of interdisciplinary therapy on lung function and pro/anti-inflammatory adipokines in asthmatic and non-asthmatic obese adolescents.

MATERIALS AND METHODS

Population

After a sample size power calculation, a total of 91 (15- to 19-year old) obese adolescents were enrolled to participate in the Interdisciplinary Obesity Program of the Universidade Federal de São Paulo-Escola Paulista de Medicina—UNIFESP—EPM (Fig. 1). The obese adolescents were classified with simple obesity (BMI >95th percentile on the CDC reference growth charts), and at the post-pubertal stage on the Tanner scale (stage 5) for both boys and girls.

The study occurred at the Sleep Institute in CEPE-GEO Obesity Interdisciplinary Program, São Paulo. The data were obtained in 2008 and 2009, when lung function was initially evaluated. Subjects were divided into two groups, asthmatic and non-asthmatic (Fig. 1). The groups were paired by age, BMI, and gender. Non-inclusion criteria were as follows: metabolic syndrome diagnosis, endocrine genetic diseases, or identified genetic diseases (evaluated based on medical history), viral diseases, previous drug use, and smoking.

This study was carried out in accordance with the principles of the Declaration of Helsinki and was formally approved by the Institutional Ethical Committee of the Universidade Federal de São Paulo—Escola Paulista de Medicina—UNIFESP—EPM (0135/04). Informed consent was obtained from all subjects and/or their parents, and participation of the adolescents and their families was voluntary.

Study Protocol and Medical Screening

Subjects were medically screened, and their pubertal stage and anthropometric measures were evaluated. For all subjects, the procedures were scheduled for the same time of day to remove any influence of diurnal variation. An endocrinologist recorded their health and medical history monthly to better management of obesity.
Anthropometric Measurements and Body Composition

Subjects were weighed while wearing light clothing and no shoes on a Filizola scale to the nearest 0.1 kg. Height was measured to the nearest 0.5 cm with a wall-mounted stadiometer (Sanny, model ES 2030). Body mass index (BMI) was calculated as body weight divided by height squared (wt/ht²).

Body composition was measured by plethysmography in a BOD POD body composition system (version 1.69; Life Measurement Instruments, Concord, CA). Visceral and subcutaneous fat were assessed by ultrasonography as previously described.

Serum Analysis

Blood samples were collected at the outpatient clinic around 8 am after an overnight fast by a skilled and qualified technician. After collection, the blood was centrifuged for 10 min at 5,000 rpm and stored at −70°C. The materials used for collection were disposable, adequately labeled, and of recognized quality. Adiponectin (Phoenix Pharmaceuticals, Belmont, CA), CRP (CHEMICON International, Inc., Millipore, Billerica, MA), and leptin (CHEMICON International, Inc., Millipore) levels were measured using a commercially available enzyme-linked immunosorbent assay (ELISA) kit according to the manufacturer’s instructions. The reference values of leptin concentration were from 1 to 20 ng/ml for boys and from 1 to 24 ng/ml for girls.

Evaluation of the Lung Function

Lung function was measured with a spirometer EasyOne model 2001 (Zurich, CH) according to American Thoracic Society criteria. The highest of three technically appropriate measurements was recorded. While performing the maneuver, volume–time and flow–volume curves were followed on the screen. Forced vital capacity (FVC, L), FEV₁ (L), FEV₁/FVC (%) and peak expiratory flow (PEF, L/sec) were measured, and predicted values were obtained.

The diagnosis of asthma was made according to ATS guidelines. Specifically, the asthmatic patients had a 6-month or longer history of recurrent chest symptoms, such as coughing, dyspnea, and wheezing, which were
relieved by bronchodilator treatment and that demonstrated reversible airflow limitation. The International Study of Asthma and Allergy in Childhood (ISAAC) questionnaire was used to assess asthma-related symptoms. Furthermore, information on anti-asthmatic medication was obtained. Medical therapy included regular use of inhaled corticosteroids or β2-agonists (data not shown). The severity of asthma was classified according to GINA criteria. The asthmatic patients were evaluated by a pulmonologist.

Research Design

A 1 year of interdisciplinary weight loss program combined exercise training with nutritional, psychological, and medical therapy. The use of interdisciplinary intervention as a criterion has been suggested by the World Health Organization. All measurements were performed at baseline and after 6 months (short-term) and 1 year (long-term) of therapy.

Psychological Therapy

During 1 year of interdisciplinary therapy, the adolescents received psychological orientation for 1 hr in a weekly group session. A psychologist discussed body image and eating disorders as well as binge eating disorders and their signs, symptoms, and health consequences. The psychologist also discussed the relationship between emotions and food as well as familial problems in a group setting. Individualized psychological therapy was recommended when behavioral alterations including depression and anxiety symptoms or poor dietary habits were found, such as bulimia, anorexia nervosa, and binge eating.

Nutritional Therapy

Once a week for 1 year, adolescents had nutritional lessons regarding such topics as the food pyramid, food record, weight loss diets, diet and light concepts, fat and cholesterol, and eating disorders. Energy intake was set at the levels recommended by the dietary reference for subjects with low levels of physical activity of the same age and gender. A 3-day dietary record was made for each adolescent to help his/her parents. Portions were measured in terms of familiar volumes and sizes. The nutritionist explained to the parents and the adolescents how to record food consumption. These dietary data were transferred to a computer by the same nutritionist, allowing for nutrient composition analysis by a PC program developed at the Universidade Federal de São Paulo—Escola Paulista de Medicina—UNIFESP—EPM (Nutwin software, for windows, 1.5 version, 2002) based on Western and local food tables.

Physical Therapy

An aerobic and resistance training regimen was performed three times a week for 1 year. Each session included 30 min of aerobic training plus 30 min of resistance training. Aerobic training consisted of running on a motor-driven treadmill (Life Fitness—Model TR 9700HR) at the cardiac frequency intensity of ventilatory threshold I (±4 bpm), which was determined by the results of an initial oxygen uptake test for aerobic exercise (cycle-ergometer and treadmill). In addition, the maximal O2 consumption (VO2 max) values were obtained from the oxygen uptake tests.

The physiologists controlled the cardiac frequency, which was measured with a cardiometer at 5 min intervals during all training sessions (Polar—Model FS1 dark blue). The exercise program was based on the American College of Sports Medicine recommendations (ACSM).

Statistical Analysis

Statistical analyses were performed using STATISTICA (version 7.0 for Windows), and a sample size calculation was performed with alpha 0.05. The Gaussian distribution of variables was verified with a Shapiro–Wilk’s W-test, and variables with normal distribution were expressed as the mean ± standard deviation (SD), while variables without normal distribution were expressed as medians (minimum and maximum) in a descriptive table. Nonparametric methods were used when appropriate.

The comparisons between the measurements of the parametric variables before intervention, 6 months and 1 year after intervention were determined by repeated measures analysis of variance (ANOVA) using correction for pairwise. The Wilcoxon signed rank and Mann–Whitney U-tests were used to analyze the nonparametric variables.

A correlation study was performed, but just as an exploratory method. Linear regression analysis was used to ascertain the predictor factors to lung function at baseline and after therapy. The FVC, FEV1, or PEF values were set as dependent variable, while, BMI, VO2 max, adiponectin, CRP, or leptin concentrations were set as independent variables in different models, where these variables were controlled by age and gender. In a second moment, a multiple regression analysis was done to evaluate the predictors factors of changes in FVC, FEV1, or PEF values after therapy, for this analysis was used the delta values of these variables, by calculating: Δ = the difference of values between 6 months or 1 year and baseline.

Furthermore, Grubb’s test was used to detect outliers, using GraphPad Prism (version 5.0 for Windows).
results were considered statistically significant at the level of \( P < 0.05 \).

**RESULTS**

At the beginning of therapy, 91 obese adolescents were enrolled in the program. However, 76 patients completed 1 year of therapy with more than 75% of presence in the treatment sessions and were divided into two groups, asthmatic (26 patients) and non-asthmatic (50 patients). It is important to note that there were no differences for all variables between those that completed the therapy and the last known data from those that did not. The main reasons for dropping out in our study were financial and family problems, followed by school and job opportunities (Fig. 1).

At baseline, we did not find significant differences in age and BMI between the groups after the studied population was paired by these variables according to gender. Furthermore, there were no statistically significant differences between genders in both groups for all variables (data not shown).

After treatment it was observed a significantly decrease in the body mass, BMI, body fat, and visceral fat, and a significant increase in fat-free mass in both groups (Table 1).

Lung function significantly increased in both groups after the therapy. However, the asthmatics continued to have significantly lower FEV\(_1\) and PEF values compared to non-asthmatic patients (Table 1). Furthermore, we observed an increase in the maximal \( O_2 \) consumption VO\(_2\) max in both groups. In addition, the asthmatics presented higher values of eosinophil count in all evaluated times, compared to non-asthmatics patients (Table 1). The asthmatic group showed a reduction in the asthma severity (Fig. 2), asthma-related symptoms, and daily rescue medication doses after treatment (Table 1). Moreover, the asthmatic patients did not present hospitalization related to asthma exacerbation during the study.

In relation to inflammatory biomarkers, the leptin and CRP concentrations reduced after 1 year of treatment (Fig. 3A and B). On the other hand, the adiponectin levels increased in both groups after 1 year of therapy (Fig. 4).

The multiple regression analysis demonstrated that VO\(_2\) max, adiponectin, and leptin concentrations were predictor factors to PEF values, while adiponectin and leptin concentrations were predictor factors to FVC values in asthmatics at baseline (Table 2). Therefore, in asthmatics at baseline was observed that each increase of 1 ng/ml in adiponectin concentration promoted an

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**TABLE 1—Anthropometric and Lung Function Variables Measured at Baseline and After Interdisciplinary Therapy in Obese Adolescents Classified by Diagnosis**

<table>
<thead>
<tr>
<th></th>
<th>Non-asthma (50)</th>
<th>Asthma (26)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>6 Months</td>
</tr>
<tr>
<td>Female (%)</td>
<td>65</td>
<td>65</td>
</tr>
<tr>
<td>Age (years)</td>
<td>17 ± 1.4</td>
<td>16 ± 1.1</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>168 ± 0.1</td>
<td>169 ± 0.07(^1)</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>101 ± 15</td>
<td>94 ± 14(^1)</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>36 ± 5</td>
<td>33 ± 5(^1)</td>
</tr>
<tr>
<td>Body fat %</td>
<td>45 ± 6</td>
<td>39 ± 7(^1)</td>
</tr>
<tr>
<td>Fat-free mass %</td>
<td>55 ± 6</td>
<td>59 ± 7(^1)</td>
</tr>
<tr>
<td>Visceral fat (cm)</td>
<td>4.1 ± 1.1</td>
<td>3.3 ± 1.0(^1)</td>
</tr>
<tr>
<td>Sub fat (cm)</td>
<td>4.0 ± 0.8</td>
<td>3.1 ± 0.5</td>
</tr>
<tr>
<td>Maximal (O_2) consumption (ml/kg/min)</td>
<td>16 ± 3</td>
<td>18 ± 4</td>
</tr>
</tbody>
</table>

### Lung function variables

<table>
<thead>
<tr>
<th></th>
<th>Non-asthma (50)</th>
<th>Asthma (26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (%)</td>
<td>95 ± 14</td>
<td>101 ± 11(^1)</td>
</tr>
<tr>
<td>FEV(_1) (%)</td>
<td>90 ± 8</td>
<td>99 ± 9(^1)</td>
</tr>
<tr>
<td>FEV(_1)/FVC (%)</td>
<td>97 ± 7</td>
<td>99 ± 6</td>
</tr>
<tr>
<td>PEF (%)</td>
<td>117 ± 19</td>
<td>104 ± 16(^1)</td>
</tr>
<tr>
<td>PEF(_{25-75}) (%)</td>
<td>94 ± 15</td>
<td>100 ± 9(^1)</td>
</tr>
</tbody>
</table>

### Symptoms\(^4\)

<table>
<thead>
<tr>
<th></th>
<th>Non-asthma (50)</th>
<th>Asthma (26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough (%)</td>
<td>17</td>
<td>6</td>
</tr>
<tr>
<td>Wheeze (%)</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>Daily rescue medication doses</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Eosinophil count</td>
<td>0.15 (0.0–0.5)</td>
<td>0.13 (0.0–1.3)</td>
</tr>
</tbody>
</table>

\(^1\)Sub, subcutaneous.  
\(^2\)Baseline versus 6 months, \( P < .05 \).  
\(^3\)Baseline versus 1 year, \( P < .05 \).  
\(^4\)ISAAC questionnaire.

*Pediatric Pulmonology*
increase of 0.44 (β adjusted) in PEF values and of 0.36 (β adjusted) in FVC values. Furthermore, each increase of 1 ml/kg/min in VO\textsubscript{2} max promoted an increase of 0.29 (β adjusted) in PEF value. On the other hand, each reduction in leptin concentration of 1 ng/ml resulted an increase of 0.53 (β adjusted) in FVC value, and of 0.55 (β adjusted) in PEF value (Table 2).

In highlight, the multiple regression analysis demonstrated that Δ adiponectin was a predictor factor to improve lung function after therapy in both groups, controlled by age and sex. Where was observed that each increase of 1 ng/ml in adiponectin concentration promoted an increase of 0.71 (β adjusted) in FEV\textsubscript{1} values in non-asthmatics and of 0.39 (β adjusted) in FVC values in asthmatics after short-term therapy (Table 3). Furthermore, after long-term therapy was showed that each increase of 1 ng/ml in adiponectin concentration promoted an increase of 0.55 (β adjusted) in FVC values in asthmatics (Table 4).

**DISCUSSION**

Few studies have examined the effect of interdisciplinary therapy on the asthmatic obese patients. In the present study, we observed that a weight loss program improved lung function, asthma severity, and inflammatory biomarkers profile in asthmatics obese adolescents. In addition, for the first time we showed that the change in adiponectin concentration was a predictor factor to improvement in lung function.

Corroborating with previous studies,\textsuperscript{32–34} we found that lung function increased paralleled by a reduction in asthma severity after the interdisciplinary therapy. This increase in FEV\textsubscript{1} and FEV\textsubscript{1}/FVC may reflect the improvement in lung volumes, a well-known effect of weight loss in obesity.\textsuperscript{32,33} Obesity adversely affects lung volumes and airflow, the underlying mechanisms may include the mechanical effects of central adiposity on lung function,\textsuperscript{3} as well as the inflammatory process associated with obesity. The adipose tissue produces inflammatory mediators with proinflammatory properties, such as leptin and CRP, and anti-inflammatory functions, such as adiponectin.\textsuperscript{24,25}

The adipocytes are the most important source of adiponectin, its serum levels are markedly decreased in individuals with visceral obesity.\textsuperscript{15} The action of adiponectin go beyond metabolic effects on glucose regulation and fatty acid metabolism; they also include an anti-inflammatory effect. The anti-inflammatory actions expand to inhibition of IL-6 production accompanied by induction of IL-10 and IL-1 receptor antagonists.\textsuperscript{16,35,36} In this sense, previous studies have demonstrated that adiponectin concentration is reduced during airway inflammation and hyperresponsiveness.\textsuperscript{16,37} On the other hand, researches that associated adipokines and asthma have documented a protective effect of high adiponectin concentration in human.\textsuperscript{38,39} Taken together, these data suggest that the reduction in
Adiponectin concentration may contribute to the pathogenesis and severity of asthma; however, the mechanisms for this interaction are not well defined. Therefore, one of the most important findings of the present study was the increase in adiponectin concentration paralleled by a reduction of asthma severity, after treatment. This reduction in asthma severity corroborates with other studies developed in adults.\(^3\),\(^3\)

Prior investigations have documented the important role of interdisciplinary treatment in the management of obesity.\(^4\),\(^1\) However, these reports did not evaluate the effects of this kind of therapy on the link between asthma and obesity-related inflammatory biomarkers. This is an important issue since recent data\(^4\) concluded that obesity associated with asthma results in a unique asthma phenotype that require a distinct therapeutic approach.\(^4\),\(^4\) Therefore, the results of our investigation demonstrated that the interdisciplinary therapy is an essential tool in the management of asthma associated with obesity and that the integrated approach is acceptable for patients with asthma.

Other highlight in the present investigation was that the proinflammatory biomarkers reduced after therapy; although they were not predictors of changes in lung function. It has been hypothesized that high levels of proinflammatory molecules released from adipose tissue into the systemic circulation could contribute to airway inflammation and increase asthma severity.\(^4\) Previous studies observed that higher CRP levels were correlated with severe asthma\(^4\) and that it could be related to asthma exacerbations and allergic inflammation.\(^4\)

### TABLE 2—Multiple Regression Analysis for the Determinant Factors of FEV\(_1\), FVC, and PEF at Baseline

<table>
<thead>
<tr>
<th>Factors</th>
<th>Non-asthma (50)</th>
<th>Asthma (26)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FVC (%)</td>
<td>FEV(_1) (%)</td>
</tr>
<tr>
<td>BMI (kg/m(^2))(^1)</td>
<td>0.37</td>
<td>0.19</td>
</tr>
<tr>
<td>Adiponectin (ng/ml)(^1)</td>
<td>0.22</td>
<td>0.63</td>
</tr>
<tr>
<td>CRP (ng/ml)(^1)</td>
<td>-0.02</td>
<td>0.16</td>
</tr>
<tr>
<td>Leptin (ng/ml)(^1)</td>
<td>-0.10</td>
<td>0.13</td>
</tr>
<tr>
<td>VO(_2) max (ml/kg/min)(^1)</td>
<td>0.42</td>
<td>0.50</td>
</tr>
</tbody>
</table>

\(^1\)Analyses controlled for age and sex.

*Pediatric Pulmonology*
Several researches have evaluated the role of leptin in the relationship between obesity and asthma. They showed a negative effect of leptin resistance or deficiency on breathing disorders, remodeling features, severity, and pathogenesis of asthma. In the present study, leptin concentration was a predictor factor to low FVC values in asthmatics obese adolescents at baseline, in agreement with other studies. Thus, in obese individuals, the biological activity of adipose tissue may worsen the asthma severity, reinforcing the importance of this kind of intervention in early life.

The sedentary state of obese individuals further complicates matters by putting an added strain on the respiratory system. Their decreased VO$_2$ max makes this system work much harder for an equivalent level of physical activity. In our study, we observed that VO$_2$ max value was a predictor factor to high PEF values in asthmatics at baseline, however, this variable was not a predictor factor to the improvement in lung function. Therefore, we suggest that in the present study, the fitness was not the main factor to ameliorate the lung function.

Future studies may also measure other inflammatory mediators including the vascular endothelial growth factor (VEGF), interferon-γ, and eotaxin levels to better delineate the mechanism involved in the link between asthma and obesity. Furthermore, studies that investigate healthcare costs related to office visits, urgent or emergent care, missed work days and years of productive life lost are needed. Another limitation of the present study was the absence of a control lean asthmatic group and/or an obese group untreated to compare important issues as placebo effect and the benefits of attention due to trial.

In conclusion, this study demonstrated an improvement in lung function, asthma severity, and inflammatory biomarkers profile in obese adolescents after interdisciplinary therapy. Furthermore, it was revealed Δ adiponectin as a predictor factor of improvement in lung function after treatment.

ACKNOWLEDGMENTS

Financial support was provided by AFIP, CNPq, CAPES, FAPESP 2008/53069-0, FAPESP 2006/00684-3, FAPESP 98/14303-3, CENESP, FADA, FAPESP (CEPID/Sleep No. 98/14303-3 to S.T.), and UNIFESP. The CEPE-GEO Obesity Interdisciplinary Program was supported by UNIFESP. Special thanks go to the patients and their parents.

### TABLE 3—Multiple Regression Analysis for the Determinants of Changes in FEV$_1$, FVC, and PEF After Short-Term Therapy

<table>
<thead>
<tr>
<th>Factors</th>
<th>Non-asthma (50)</th>
<th>Asthma (26)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ΔFVC (%)</td>
<td>ΔFEV$_1$ (%)</td>
</tr>
<tr>
<td>β</td>
<td>P-value</td>
<td>β</td>
</tr>
<tr>
<td>ΔBMI (kg/m$^2$)$^1$</td>
<td>–0.67 0.55</td>
<td>1.08 0.12</td>
</tr>
<tr>
<td>ΔAdiponectin (ng/ml)$^1$</td>
<td>0.28 0.78</td>
<td>1.67 0.00</td>
</tr>
<tr>
<td>ΔCRP (ng/ml)</td>
<td>0.00 0.31</td>
<td>–0.00 0.10</td>
</tr>
<tr>
<td>ΔLeptin (ng/ml)$^1$</td>
<td>0.01 0.90</td>
<td>–0.07 0.36</td>
</tr>
<tr>
<td>ΔVO$_2$ max (ml/kg/min)$^1$</td>
<td>0.26 0.74</td>
<td>0.45 0.39</td>
</tr>
</tbody>
</table>

$^1$Analyses controlled for age and sex.

### TABLE 4—Multiple Regression Analysis for the Determinants of Changes in FEV$_1$, FVC, and PEF After Long-Term Therapy

<table>
<thead>
<tr>
<th>Factors</th>
<th>Non-asthma (50)</th>
<th>Asthma (26)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>ΔFVC (%)</td>
<td>ΔFEV$_1$ (%)</td>
</tr>
<tr>
<td>β</td>
<td>P-value</td>
<td>β</td>
</tr>
<tr>
<td>ΔBMI (kg/m$^2$)$^1$</td>
<td>0.89 0.27</td>
<td>1.49 0.20</td>
</tr>
<tr>
<td>ΔAdiponectin (ng/ml)$^1$</td>
<td>–0.37 0.76</td>
<td>0.89 0.71</td>
</tr>
<tr>
<td>ΔCRP (ng/ml)</td>
<td>0.00 0.77</td>
<td>0.00 0.40</td>
</tr>
<tr>
<td>ΔLeptin (ng/ml)$^1$</td>
<td>0.02 0.81</td>
<td>0.03 0.88</td>
</tr>
<tr>
<td>ΔVO$_2$ max (ml/kg/min)$^1$</td>
<td>0.81 0.71</td>
<td>0.87 0.71</td>
</tr>
</tbody>
</table>

Analyses controlled for age and sex.
REFERENCES


Biomarkers and Lung Function in Asthmatic Obese