Exercise induced bronchospasm in asthmatic and non-asthmatic obese children


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SUMMARY

Aim: to investigate the spirometric response to the exercise challenge in asthmatic and non-asthmatic obese children.

Patients, materials and methods: it was a prospective, longitudinal, open label clinical trial with four groups of children from 8 to 16 years. The group 1 had 15 asthmatic non-obese children. The group 2 had 15 asthmatic obese children. The group 3 had 15 non-asthmatic obese children. The group 4 had 13 control healthy children. Spirometry measures were realized at baseline, and after exercise at 2, 5, 10, 15, 20, 25, 30 and 60 minutes. Exercise challenge was performed on a walking band at 6 km/h speed and a slope of 10° with a duration of 6 to 8 minutes. Data were analyzed by repeated measures ANOVA.

Results: the mean age was 11.8 ± 2.1, and the mean height was 150.2 ± 11.3 cm, the mean weight was 46.3 ± 17.15 in the group 1, 59.4 ± 11.9 in the group 2, 67.8 ± 20.6 in the group 3, and 44.2 ± 9.7 in the group 4. The mean values of forced expiratory volume in one second (FEV₁) for each group are shown on table II.

Conclusions: the non-asthmatic obese children had a significant decrease in FEV₁, meanwhile the asthmatic obese children had a deeper decrease in FEV₁ than the asthmatic non-obese children. Obesity may be a conditioning factor for bronchial hyperreactivity to the exercise.

Key words: Obese children. Exercise-induced bronchospasm. Bronchial hyperreactivity.


INTRODUCTION

During the last decade there has been a marked increased in obesity among children (1) probably secondary to incorrect alimentary habits or a limited physical activity (TV, videogames, etc.). The pediatric obesity natural history is not completely known and still has to be clarified. Binkin et al (2) have shown a specific relationship between birth weight and obesity in adulthood. Some studies associate the adult obesity, with the weight gained on the first year of life and with the infant obesity (3-5).

Similarly, obese children have important reductions in expiratory reserve volume (ERV), forced expiratory volume in one second (FEV₁), forced expiratory flow between 25 and 75% of vital capacity (FEF₂₅-₇₅) and maximal voluntary ventilation (MVV) (4-6). Additionally, an early report indicates that obese children suffer bronchospasm after exercise challenge with falls in FEV₁ and FEF₂₅-₇₅ with a pattern similar to the asthmatic patients (7).

These data suggest that the period of life from the first year up to the fifth year of age can be critical for the development of massive obesity in adulthood (3, 5). Obesity in puberty is related to an increased morbidity and mortality rates over the expected in adult (1, 8) causing a significant detrimental on health becoming a cardiovascular risk, like hypertension, hypercholesterolemia or diabetes. The pediatric population with obesity is associated with hypertension, respiratory diseases, diabetes and orthopedic alterations (1).

Excessive body fat can directly cause harmful effects over the ventilatory function, like thorax wall alterations (changes on compliance), on the diaphragm (not allowing its downward movement
inside the abdominal cavity), on the ventilatory work (ventilatory muscles) and elasticity (9-12). In accordance to the pattern of body fat distribution, superior obesity (thorax and abdomen) originates an increment on the resistance and has been related with compromised pulmonary volumes, showed as exercise dyspnea. This is important on male adults, because is one of the explanations for the respiratory disorders (8). But is not truly by Shaheen (13) who said that the prevalence of adult asthma increased as increase the BMI, particularly in women.

Minority children suffering overweight have a higher prevalence of asthma than their matched controls (4), and the children with asthma are more overweight than the controls without asthma. Overweight children have a higher risk for low expiratory flow rate (PEFR) and more prescriptions of asthma medications.

Body fat distribution is not similar among children and adolescents so Fung et al (11) consider that obesity and its pulmonary repercussions, correlates with the body mass index (BMI = weight / height^2) with a direct relation on decreased pulmonary volumes. Therefore when pulmonary function is evaluated, it is essential to consider the BMI, because when its over 25 (obesity) a diminution of the pulmonary volumes is expected.

It’s will known that asthma prevalence and obesity had increased. The Third Health and Nutrition Reunion showed a rise of 45.2% and 42.2% of overweight on male and female children respectively between 6 and 17 years old (1).

Bronchial hyperresponsiveness, the principal mechanisms of asthma physiopathology, can be triggered by different ways like aeroalergens inhalation, chemical irritants, pollution and exercise.

Exercise induced bronchospasm is observed on more than 80% of asthmatic patients, this exercise hyperresponsiveness is due to osmolarity changes (hyperosmolarity) causing degranulation of mast cells that release inflammatory enzymes leading to a bronchoconstrictor effect (15).

From a clinical approach, more symptoms have been reported on asthmatic patients with obesity than non obese ones (1, 7, 16). Overweight in children and exercise have been related with cough, wheezing, dyspnea and thoracic oppression but these complaints had been awarded to their poor physical condition.

Due to the importance that obesity has, by its sistemic and respiratory repercussions and by the barely number of pulmonary function test trials, we decide to investigate the bronchial response to exercise challenge on obese asthmatic and non asthmatic patients compared with asthmatic non obese and healthy patients, and then the aim of this study was to asses the effect of obesity in the ventilatory function of children suffering asthma after an exercise challenge.

**MATERIALS AND METHODS**

A prospective, longitudinal, open trial was carried out on 58 pediatric patients between 8 and 16 years old and assigned to four groups according to their weight and clinical status: group 1) fifteen non obese asthmatic patients with body weight (BW) between 25-75th percentile (obtained from the National Center for Health Statistics) and BMI between 15-20 kg/m^2. Group II) fifteen asthmatic obese patients with BW > 95th percentile, BMI over 25 and overweight greater than 120% (more than 20% of ideal body weight). Group III) fifteen obese non asthmatic patients with BW > 95th percentile, BMI over 25 kg/m^2 and overweight greater than 120% (more than 20% of ideal body weight), d) fifteen healthy patients with BW between 25-75th percentile and BMI between 15-25 kg/m^2.

To be eligible to participate in the study the non asthmatic patients (obese and non obese) must have no family history of atopy and no records of cough, wheezing or dyspnea suggesting asthma. The asthmatic patients (obese and non obese) must be clinically stable. All patients must be without immunotherapy, no regular use of sodium cromoglicate or corticosteroids at least 2 months prior the beggining of the study, without upper respiratory infection within 6 weeks before the study, without asthma exacerbation within 9 weeks before the study, without cardiovascular or concomitant pulmonary diseases, without musculoskeletal or neurologic disorders and with initial forced expiratory volume in one second (FEV1) more than or equal to 80% of base predicted, according to Pérez Neria tables (17). Informed consent was obtained from the parents and a medical history, physical examination, vital signs, thorax X-ray, and EKG was performed to all patients, who were normals.

The trial subjects should have no physical exercise or food intake before the exercise challenge.

Because of exercise challenge represents a risk for susceptible patients, an emergency kit and oxygen delivery system for nebulizations was ready anytime.

Exercise challenge was performed on an area of 10 × 10 m^2 with a room temperature between 22-24° C, a relative humidity of 40% and between 14

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and 16 hours of the day. Patients must refrain from strenuous exercise for 48 hours before exercise challenge and no food intake 4 hours before the test. After a full explanation and with comfortable clothes the patient exercised on a treadmill (Quinton instruments made in USA) starting at a speed of 1 km/h and a gradient of 0% of its total inclination, increasing 1.5 km/h and 2.5% of inclination each 30 seconds for 2 minutes till reach 6 km/h and 10% of its total inclination. When patients achieved their submaximal heart rate (210-age × 0.65), they continued for 4 more minutes with the same workload. The average time for the exercise challenge was 6 to 8 minutes (18-19). The test was interrupted if severe dyspnea, cyanosis or thoracic pain appear regardless of respiratory function values.

A standard spirometer (Vitalograph model FP 239 made in USA) was used. Spirometry was performed before the challenge to set up a basal value (best of three maneuvers) and at 2, 5, 10, 15, 20, 25, 30 and 60 minutes after exercise. FEV₁ and FEF₂₅₋₇₅ were considered unaltered if they were ≥ 95% of the baseline values. Whenever a decreased of 5% of the baseline values was detected, the spirometry was repeated and the best of the two measures was taken. A positive test was considered, when a patient showed a drop of the FEV₁ > 15% from the baseline value, and/or clinical criteria like; wheezing, severe dyspnea, cyanosis, arrhythmia or thoracic pain. The positive value for the FEF₂₅₋₇₅ was a decreased > 25%. Patients that did not showed a fall on FEV₁ > 15% and without shortness of breath continued their spirometric maneuvers until finishing their observation hour.

All the patients that had clinical bronchospasm symptoms or fall on FEV₁ > 15% from their baseline received inhaled albuterol (100 mcg on two doses) with a metered dose inhaler and a spacer.

The demographic and anthropometric variables were compared by analysis of variance and the spirometry measures by the analysis of variance for repeated measures.

RESULTS

Age and height were similar on all groups with no significative differences (p > 0.5), as shown in table I. Whereas weight, overweight % and BMI used to classify each group were significantly different (p < 0.01) on the obese asthmatics compared with asthmatics non obese and with healthy ones with weight (59.4 ± 11.9 vs 46.3 ± 10.7 and 44 ± 9.7), BMI (30.5 ± 3.5 vs 19.5 ± 3.5 and 19.3 ± 3) and overweight % (167 ± 37.5 vs 96.5 ± 15 and 98 ± 13) respectively, without significative difference (p > 0.5) between both obese groups (table I).

Male sex predominate 2:1 on groups 1, 2 and 3 (asthmatics non obese, obese asthmatics and obeses non asthmatics) but not in group 4 that were similar.

As seen on table II the mean values of FEV₁ in all groups with the exception of group 4 (healthy), showed a significative decreased (p < 0.001) compared with their base line. The obese non asthmatics showed similar values than the asthmatic non obese (Fig. 1).

Analizing each group by itself, we found that on the asthmatic non obese children, the FEV₁ base line decreased more than 15% on 12 patients (80%) (clasifying them as exercise hyperresponsiveness), and in the obese asthmatics all were positive 15/15 (100%). The obese non asthmatics and asthmatic non obese behave similar with 73.3% (11/15) with exercised induced bronchial hiperresponsiveness without previous history of asthma (Fig. 2).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Age</th>
<th>Weight</th>
<th>Height</th>
<th>BMI</th>
<th>% overweight</th>
</tr>
</thead>
<tbody>
<tr>
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<td>12.6 ± 1.4</td>
<td>46.3 ± 10.79</td>
<td>152.3 ± 3.5</td>
<td>19.5 ± 3.5</td>
<td>0</td>
</tr>
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<td>2</td>
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<td>59.4 ± 11.9</td>
<td>148 ± 10.8</td>
<td>30.5 ± 3.5</td>
<td>67 ± 37.5</td>
</tr>
<tr>
<td>3</td>
<td>11.4 ± 2.0</td>
<td>67.8 ± 20.6</td>
<td>149 ± 12.3</td>
<td>31.5 ± 5.5</td>
<td>70 ± 45</td>
</tr>
<tr>
<td>4</td>
<td>11.8 ± 2.6</td>
<td>44.0 ± 9.7</td>
<td>150 ± 11.2</td>
<td>19.3 ± 3.5</td>
<td>0</td>
</tr>
</tbody>
</table>

Group 1 asthma non obese and group 4 healthy = p > 0.05. Group 2 asthma obese and group 3 obese p > 0.05.

| Table I |

Mean values of age, weigh, size and IMC in exercise induced bronchospasm in asthmatic and non-asthmatic obese children in 4 groups of the children

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The drop of FEV\textsubscript{1} > 15% observed on asthmatic non obese 60% (9/15) and obese ones 53.3% (8/15) started between 10 and 20 minutes whereas obese non asthmatics had any correlation of time. The recovery of the FEV\textsubscript{1} started at 30 minutes without reaching the baseline values in all groups except healthy ones (Fig. 3).

On the other hand, the FEF\textsubscript{25-75} values showed a statistically significative disminution (p < 0.001) especially on the obese asthmatic group. As figured on figure 2, the disminution of FEF\textsubscript{25-75} > 25% was of 66% (10/15) on the obese asthmatics, compared with 40% (6/15) of the asthmatic non obese and with 33% (5/15) of the obese non asthmatics. Interestingly, earlier changes were noted on the FEF\textsubscript{25-75} over the FEV\textsubscript{1} (2 to 10 minutes) principally on the obese asthmatic group.

Regarding to the symptoms, cough was present on 60% (9/15) of the obese asthmatic group, followed by 53% (8/15) of the asthmatic non obese, 20% (3/15) on obese non asthmatics and 15% (2/13) on the healthy group. Wheezing appeared on asthmatic non obese and obese non asthmatic on 40% (6/15) and 66% (10/15) respectively and dyspnea also appeared on asthmatic non obese and obese non asthmatic 2 and 1 respectively (Fig. 4).

The spirometric maneuvers were interrupted on three patients from the asthmatic non obese group (two at 5 minutes and one at 10 minutes) and on 4 patients from the asthmatic obese group (two at 2 minutes, one at 15 minutes and one at 20 minutes) because a drop greater than 20% on FEV\textsubscript{1} with wheezing and dyspnea.

**DISCUSSION**

Two epidemics are affecting children by the end of the XX century; obesity and asthma. Overweight children are more frequently affected by asthma than non-overweight controls and asthmatic children are more overweight than the non-asthmatic controls.

The effects of massive obesity over the respiratory function has been plenty studied in adults. Obese subjects tend to have decreased pulmonary volumes and less thoracic wall distensibility (11). However,
few studies of pulmonary function in obese children and even less ones in obese asthmatics had been informed.

The aim of this study was to establish the effect of obesity in the ventilatory function of children suffering asthma after an exercise challenge.

Obese, asthmatic children had a worse response to the exercise than the non-obese, asthmatic children regarding falls in FEV\textsubscript{1} and FEF\textsubscript{25-75}, and symptomatology.

Obese children presented important decreases in FEV\textsubscript{1} and FEF\textsubscript{25-75} with a pattern similar to the asthmatic patients.

Obesity worsen the condition of the asthmatic children, and obesity is a risk factor for a positive exercise challenge assessment a probably to develop asthma.

The body fat distribution in children and adolescents is different than the adult. On the first ones and particularly on girls, the fat is placed on extremities rather than on trunk, so the respiratory function on these groups is not affected inversely and no negative correlation between BMI and pulmonary function is seen. In them, the BMI is not a merely reflection of fat tissue because it can’t differentiate between muscles, bone and fat, and a positive correlation between BMI and respiratory function strength (the amount of effort put into doing the maneuvers). However, on obese subjects or overweighted, the BMI can reflect the real adipocity, therefore, is necessary to use the BMI (weight/height\textsuperscript{2}) to assess obesity and its repercussion on respiratory function on the obese children (9, 11, 20).

Fung et al (11) showed a negative relationship between BMI and the FEV\textsubscript{1} and FEF\textsubscript{25-75}, specially on boys probably due to abdominal fat accumulation on male rather than female children. Our findings does not agree, probably because the large number of female patients included.

Kaplan (7) confirms the bronchial hiperresponsiveness due to exercise (decreased FEV\textsubscript{1} and FEF\textsubscript{25-75}) in obese children over de 95th percentile vs healthy children, finding a greater relationship between obesity and FEF\textsubscript{25-75}, therefore he concludes that the predominante effect for the exercise induced bronchospasm on obese children affects more the small-airways.

In our study comparing different groups (healthy, asthmatic non obese and obese asthmatics and non asthmatics), we found that FEF\textsubscript{25-75} decreased earlier (2-10 minutes) after exercise only in the asthmatic obese ones, while the obese non asthmatics showed a similar pattern of the asthmatic non obese (between 5 and 30 minutes). As expected, exercise induced bronchospasm cause a drop of FEV\textsubscript{1} in most of the asthmatic obese and non obese between 2 and 15 minutes. The obese non asthmatics showed a similar pattern of the asthmatic non obese too. The mayor drop of FEV\textsubscript{1} and FEF\textsubscript{25-75} was noticed in the asthmatic obese group and anyone from the healthy group. The BMI correlate negatively with the decreased FEV\textsubscript{1} and FEF\textsubscript{25-75} in the obese group. It has been reported that asthma can help children to gain weight due to its limitated physical activity (up to 18% of decremental physical activity under 18 years), likewise the overweight can exacerbate the asthma symptoms through an effect respiratory function (1, 7).

Our study confirms a positive correlation between BMI and its repercussion on the symptoms (cough, wheezing and dyspnea) of the asthmatic children, as described by Luder et al (1) and Schwartz et al (21), because the asthmatic obese group, followed by the asthmatic non obese had more symptoms triggered...
by exercise, while the obese non asthmatics and healthy had similar number of symptoms.

Once proved that —like in other trials— the relationship between the BMI and its respiratory function repercussion in obese asthmatic and non asthmatic children, raises the question of whether having exercise induced bronchospasm predisposes a child for developing obesity by avoiding aerobic exercise or whether obesity leads to or exacerbates exercise induced bronchospasm by some physiologic, biochemical or emotional mechanism.

Asthma severity can contribute to overweight, and sometimes is conditioned by parents that limit the physical activity of their children believing that asthmatic people must not practice exercise, bringing them to a sedentary life. One hypothesis is that hyperreactivity leads to avoid exercise which in turns caused a positive energy balance and overweight, other hypothesis is that the lack of exercise in the obese provokes a low response of the airways, and finally that a low sympathetic tone is a common risk factor for asthma and obesity.

Probably in the obese non asthmatic subjects, exist a disturbance on the adrenergic regulation of the adipocyte metabolism, causing an alfa-adrenergic stimulation for lipogenesis (22).

Another possibility for the link between asthma and obesity is the low sympathetic tone. Due to obesity has been associated to the low sympathetic tone, which provokes lower energy expenditure, a positive energy balance and fat accumulation (22, 23). Enhanced, parasympathetic activity is a factor in the pathogenesis of asthma (24) and heart rate variability, a marker of sympathetic activity, is lower in asymptomatic and symptomatic asthmatic patients than the controls (25, 26).

An alternative explanation is that the weight gain due to the use of drugs for the treatment of asthma such as corticoids and antihistaminics but the selected patients in this trial not used this sort of drugs.

In summary, the exercise challenge affects more the asthmatic obese patients than the asthmatic non obese by the additional overweight, causing a detrimental over the respiratory function. Thus, the patients obese without asthma were affected on the same way than asthmatic non obese, therefore, the greater BMI, the fewer pulmonary response (fall on FEV\textsubscript{1} and FEF\textsubscript{25-75}).

We conclude that it is necessary to reduce overweight on asthmatic and non asthmatic patients to improve their ventilatory function and to obtain a better quality of life.

This study has two corollaries; the control of overweight must be part of the management of the management of the asthmatic children; and the prevention of asthma must consider the prevention of the overweight.

Further studies should be planned to elucidate the role of obesity in the pathogenesis of asthma.

RESUMEN

La obesidad en el niño se ha incrementado en la última década. Desafortunadamente las alteraciones de la función pulmonar han sido poco estudiadas en niños obesos con y sin patología respiratoria como el asma. Nuestro objetivo fue evaluar la función pulmonar al reto con ejercicio en niños obesos con asma y sin asma. Se realizó un estudio prospectivo, longitudinal, abierto, en 58 niños de 8 a 16 años, divididos en cuatro grupos: grupo 1 (15 asmáticos no obesos), grupo 2 (15 asmáticos obesos), grupo 3 (15 obesos no asmáticos) y grupo 4 (13 niños sanos). Antes de iniciar el reto con ejercicio se realizó una espirometría basal y posteriormente a los 2', 5', 10', 15', 20', 25', 30' y 60'. La prueba de ejercicio fue en una banda sin fin con una velocidad inicial de 1 km/h y una inclinación de 0° hasta llegar a 6 km/h y 10° por 6 a 8'. Cuando el FEV\textsubscript{1} disminuía más del 15% de los valores basales y/o tenían síntomas y tos se consideraba que el paciente presentaba una obstrucción de la vía aérea de gran calibre, diagnosticándose así broncoespasmo inducido por ejercicio. El estudio estadístico fue mediante el análisis de varianza de medidas repetidas.

Resultados: la edad media de los cuatro grupos fue de 11,8 ± 2,1 años y la talla de 150 ± 11,3 cm. De acuerdo a cada grupo el peso medio del grupo 1 fue de 46,3 ± 17,1 kg, grupo 2: 59,4 ± 11,9, grupo 3: 67,8 ± 20,64 y grupo 4: 44,2 ± 9,7 kg. El descenso del FEV\textsubscript{1} fue de 46,3 ± 17,1 kg, grupo 2: 59,4 ± 11,9, grupo 3: 67,8 ± 20,64 y grupo 4: 44,2 ± 9,7 kg. El descenso del FEV\textsubscript{1} mayor del 15% después del ejercicio se presentó en el 80% (12/15) del grupo 1, en el 100% del 2, en el 73,3% (11/15) del grupo 3 y en 1 de los 13 del grupo 4. De acuerdo con esto, los obesos no asmáticos tuvieron una respuesta al ejercicio semejante a los asmáticos no obesos (p = 0,05) y los obesos asmáticos respondieron más al ejercicio comparado con los asmáticos no obesos (p < 0,01) (tabla II).

Conclusiones: la obesidad es un factor que condiciona una mayor respuesta bronquial al ejercicio tanto en niños asmáticos como no asmáticos y es de llamar la atención que los obesos sin asma tengan hiperreactividad bronquial al ejercicio semejante a la de los asmáticos no obesos.

Palabras clave: Obesidad infantil. Broncoespasmo inducido por ejercicio. Hiperreactividad bronquial.
REFERENCES
