Exercise-induced bronchospasm in obese and non-obese asthmatic adolescents

Broncoespasmo induzido pelo exercício em adolescentes asmáticos obesos e não-obesos

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RESUMO

Objetivo: Avaliar e comparar a frequência e intensidade do broncoespasmo induzido pelo exercício (BIE) em adolescentes asmáticos obesos e não-obesos.

Métodos: Estudo transversal e descritivo realizado com 39 adolescentes de ambos os sexos, com idade entre dez e 16 anos, divididos em dois grupos conforme o histórico clínico de asma e/ou rinite alérgica e o índice de massa corporal: asmáticos obesos (n=18); asmáticos não-obesos (n=21). Utilizou-se o teste de broncoprovocação com exercício para a avaliação do BIE, considerando-se positiva uma diminuição do volume expiratório forçado no primeiro segundo (VEF_1) ≥15% do valor pré-exercício. Para avaliar a intensidade e a recuperação do BIE, foram calculadas a queda percentual máxima do VEF_1 ($QM\%VEF_1$) e a área acima da curva (AAC_{0-30}). A análise estatística utilizou o teste exato de Fischer para comparar a frequência de BIE e o teste de Mann-Whitney para a intensidade e recuperação. Rejeitou-se a hipótese de nulidade se $p<0,05$.

Resultados: Não houve diferença significativa na frequência de BIE entre os grupos de asmáticos obesos (50%) e não-obesos (38%). Entretanto, a queda máxima do VEF_1 e a AAC_{0-30} foram maiores nos asmáticos obesos em comparação aos não-obesos (respectivamente 37,7% e 455 *versus* 24,5% e 214, $p\leq0,03$).

Conclusões: A obesidade não contribuiu para o aumento da frequência do BIE em asmáticos e não-asmáticos, entretanto, a obesidade contribuiu para o aumento da intensidade e do tempo de recuperação da crise de BIE em asmáticos.

Palavras-chave: asma; asma induzida por exercício; obesidade; sobrepeso; adolescente.

ABSTRACT

Objective: To assess and compare the frequency and severity of exercise-induced bronchospasm (EIB) in obese and non-obese asthmatic adolescents.

Methods: Cross-sectional and descriptive study with 39 subjects aged ten to 16 years of both genders divided into two groups according to clinical history of asthma and/or allergic rhinitis and body mass index, as follows: asthmatic obese (n=18) and asthmatic non-obese (n=21). An exercise bronchoprovocation test was applied to diagnose EIB and was considered positive if the forced expiratory volume in one second (FEV_1) decreased ≥15% in relation to pre-exercise FEV_1. Maximum percent of fall in FEV_1 ($MF\%FEV_1$) and the area above the curve (AAC_{0-30}) were calculated to evaluate the intensity and recovery of EIB. Fisher exact test was used to compare the frequency of EIB and Mann-Whitney test to compare the severity and recovery of EIB. Null hypothesis was rejected when $p<0.05$.

Results: No significant difference was found in the frequency of EIB between the asthmatic obese (50%) and non-obese (38%) adolescents. However, the $MF\%FEV_1$ and AAC_{0-30} were significantly higher in the asthmatic obese as compared to the asthmatic non-obese patients (respectively, 37.7% and 455 *versus* 24.5% e 214, $p\leq0.03$).

Conclusions: Obesity did not contribute to the increase of the frequency of EIB in asthmatic and non-asthmatic patients. However, obesity contributed to the increase of severity and recovery time of EIB in asthmatics.

Key-words: asthma; asthma, exercise-induced; obesity; overweight; adolescent.

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Introduction

Obesity is a public health problem in most developed[1] and developing[2] countries. Overweight and obesity are considered to be risk factors for the development of chronic degenerative diseases such as cardiovascular diseases, type 2 diabetes, and certain types of cancer[3].

Overweight has been associated with chronic respiratory conditions such as asthma[4,5]. Excessive accumulation of adipose tissue in the central region may change the pulmonary mechanics[6], leading to an increase in the constriction and responsiveness of bronchial smooth muscles[7]. In addition, adipose cells produce inflammatory mediators that may change the airway response at high levels[8].

Most studies that have investigated the association between obesity and asthma used the respiratory symptoms to establish the clinical diagnosis of asthma[9,10]. Such procedure impairs the results because many individuals are classified as asthmatics even when there is no evidence of bronchial hyperresponsiveness (BHR)[11]. BHR, used to directly assess asthma, is a useful measure that makes it possible to understand the relation between these diseases; however, the assessment of BHR in obese individuals has shown conflicting results[12]. Urger *et al*[13] found a higher frequency of exercise-induced bronchospasm (EIB) in obese children and adolescents without a history of asthma. On the other hand, studies involving children and adolescents with a positive[14,15] or negative[16,17] history of asthma did not find any differences in the frequency of EIB between obese and non-obese subjects.

Overweight is associated with the severity of asthma, suggesting that obese asthmatic individuals have more severe exacerbation of the asthmatic crises and higher use of medication compared to non-obese individuals[18,19]. Severity of EIB, using a parameter such as the maximum decrease in the forced expiratory volume in the first second ($MDFEV_1$), has been rarely investigated and there are discordant results[13-17]. Therefore, the objective of the present study was to assess and compare the frequency and severity of EIB in obese and non-obese asthmatic adolescents.

Method

Cross-sectional descriptive study comprising 39 individuals aged between ten and 16 years. We used convenience sampling to choose the participants, who were selected from the Outpatient Clinics of Obesity of the Endocrinology and Pediatric Allergy Unit of Hospital de Clínicas de Curitiba and from public schools located nearby the hospital.

Overweight adolescents due to endocrine disorders or syndromic diseases, those who were unable to exercise in a treadmill because of motor or neurological disorders, smokers, those who had neurological and psychomotor deficit or difficulty to understand the instructions regarding the spirometric test were excluded from the study.

Participants were divided into two groups according to their body mass index (BMI) and clinical history of asthma and/or allergic rhinitis. The obese asthmatic group included 18 individuals with BMI ≥ P85 with asthma and/or rhinitis and the non-obese asthmatic group was comprised of 21 subjects with BMI < P85 with asthma and/or rhinitis.

We used BMI to classify obesity based on the cutoff points suggested by Conde and Monteiro[20]. Diagnosis of asthma was established according to the recommendations of the 3rd Brazilian Consensus on Asthma Management[21] and the consensus on allergic rhinitis based on the guidelines of the 2nd Brazilian Consensus on Rhinitis[22]. The study protocol was approved by the Research Ethics Committee of Hospital de Clínicas of Universidade Federal do Paraná, in compliance with resolution 196/96. All participants were assessed by a multidisciplinary team after their parents or guardians signed a written consent form.

BHR was evaluated using an exercise bronchoprovocation test. The parameter of pulmonary function measured was the forced expiratory volume in the first second (FEV_1) before and after exercising (3, 5, 10, 15, and 30 minutes). Physical exercise was performed in a treadmill (Series 2000 Treadmill, Marquette, USA) during 8 minutes at an intensity ≥85% of the maximum heart rate measured in a previous cardiac stress test. The speed of the treadmill was estimated using the equation: S (mph): 1.16 + 0.02 x height (cm) and the treadmill slope ranged from 10 to 15%. Both speed and slope were adjusted by the researcher until the individual reached the heart rate intended. Heart rate was monitored by a frequency meter (Polar A1, Polar Eletro, Finland). The tests were carried out during the afternoon, from 2 to 5 pm, and the temperature and humidity of the environment were controlled, with temperatures between 20 and 25°C and humidity lower than 50%.

Participants were instructed not to take coffee, tea, or soft drinks containing caffeine two hours prior to the test, to stop using short- and long-acting bronchodilators 12 hours before the test and to stop using short- and long-acting antihistamines, respectively, 48 hours and five days before

the test. In order to be able to take the test, participants should not have had any symptoms compatible with viral infection (cold or flu) in the last four weeks and should not be going through an asthmatic crisis, showing values of FEV_1 ≥80% of expected and FEV_1/FVC relation ≥ 75%[23]. The expected values of FEV_1 were those suggested by Polgar e Promodhat[24].

We used the percentage decrease of post-exercise FEV_1 compared to the pre-exercise value calculated based on the following formula to establish the diagnosis of EIB: $\%FEV_1 = (FEV_{1pre\text{-}exercise} - FEV_{1post\text{-}exercise}/FEV_{1pre\text{-}exercise}) \times 100$. A decrease of ≥ 15%[25] was considered to be positive for EIB.

The maximum percent of decrease in FEV_1 ($MD\%FEV_1$) and the area above the curve ($AAC_{0\text{-}30}$) were used to evaluate the intensity of EIB. The $AAC_{0\text{-}30}$ was calculated based on the values of the percentage of decrease in FEV_1 at the sequential times of assessment after the exercise, using the trapezoidal method. This parameter represents the combination between the maximum decrease and the recovery time of FEV_1[26].

The characteristics of the sample and the post-exercise pulmonary function were expressed as mean and standard deviation and compared using Student's *t* test. The EIB frequencies were expressed as absolute and relative frequency and compared using Fisher's exact test[27]. The analysis was performed using the computer program Statistica 6.0 and the significance level was set at α=5%.

Results

Table 1 shows the anthropometric characteristics and the initial pulmonary function of the groups. Body weight and BMI were significantly higher in the obese asthmatic group due to overweight. Initial pulmonary function was similar between the groups, suggesting that none of the groups was going through an asthmatic crisis.

EIB occurred in nine adolescents (50%) of the obese asthmatic group and in eight (38%) of the non-obese asthmatic group. There was no significant difference in the EIB frequency between the groups (p=0.42).

$MD\%FEV_1$ and $AAC_{0\text{-}30}$ were significantly higher in the obese asthmatic group when compared to the non-obese asthmatic group (Table 2).

Discussion

Overweight is associated with a large number of physiologic changes that mediate the relationship between obesity and asthma[8]. Obese individuals have systemic inflammation, with increased proinflammatory cytokines and chemokines, such as interleukin-6, leptin, interleukin-18, and tumor necrosis factor, involved in the etiology of non-atopic conditions like cardiovascular diseases, diabetes, and potentially asthma[4,5].

Obesity is not clearly associated with allergy[12]. Overweight, however, enhances the non-eosinophilic inflamma-

Table 1 – Anthropometric characteristics and pulmonary function of the groups

	Obese asthmatics (n=18)	Non-obese asthmatics (n=21)	*p*-value
Age (years)	12.0±1.5	13.7±1.7	NS
Sex (M/F)	8/10	14/7	NS
Height (cm)	157.0±8.7	158.5±9.6	NS
Weight (kg)	71.6±14.2	46.5±9.6*	<0.0001
BMI ($kg.m^{-2}$)	28.9±4.9	18.4±2.0*	<0.0001
FEV_1 (L)	2.83±0.7	2.95±0.8	NS
FEV_1 (% expected)	95±11	96±10	NS

BMI: body mass index; FEV_1: forced expiratory volume in the first second.

Table 2 – Frequency of exercise-induced bronchospasm, intensity of decrease in FEV_1 and area above the curve in the different groups studied

	Obese asthmatics (n=18)	Non-obese asthmatics (n=21)	*p*-value
$MD\%FEV_1$ (m±sd)	37.7±18.5	24.5±8.3	0.02
$AAC_{0\text{-}30}$ (m±sd)	455±469	214±275	0.03

$MD\%FEV_1$: maximum percentage decrease in FEV_1; $AAC_{0\text{-}30}$: area above the curve.

tory process and increases the risk of non-atopic asthma[8]. The values of FEV_1 and forced vital capacity (FVC) are often reduced in obese adults[7]; however, in children and adolescents, the values are similar in obese and non-obese individuals[10]. In the present study, the obese asthmatic and non-obese asthmatic subjects had similar initial values of FEV_1.

The effects of obesity can also be evidenced by the changes in the airway response, since increased body weight has been prospectively associated with increased BHR in asthmatic and non-asthmatic children[7]. Studies that have assessed the EIB frequency in obese and non-obese children and adolescents and in obese asthmatics and non-obese asthmatics have found conflicting results. Ulger *et al*[13] found a significantly higher EIB frequency in obese individuals in comparison with non-obese individuals without a history of asthma (31.6 *versus* 3.3%, p=0.003). Other studies[16,17] have not found any differences in the prevalence of EIB between obese and non-obese and obese asthmatic and non-obese asthmatic individuals[14,15]. In the present study, there was no difference in the prevalence of EIB between obese and non-obese asthmatics (50 *versus* 38.0%, p=0.42).

Overweight is associated with higher severity of asthma, since obese individuals have more severe exacerbation of the asthmatic crises and need to use more medications compared to the non-obese individuals[18,19]. Kaplan and Montana[16] found a significantly higher MD%FEV_1 in obese non-asthmatic children in comparison with non-obese children (10.4 *versus* 4.1%, p<0.05). Del Rio-Navarro *et al*[14] showed a higher MD%FEV_1 in obese asthmatic children compared with non-obese children (17.4 *versus* 9.0%, p<0.05). On the other hand, Rodrigues *et al*[15] did not find any differences between obese and non-obese asthmatic individuals. In the present study, MD%FEV_1 was significantly higher in obese asthmatics in comparison with non-obese asthmatics (37.7 *versus* 24.5%, p=0.02).

None of the studies that investigated EIB in obese adolescents used the AAC_{0-30} as a parameter for EIB. The AAC_{0-30} shows the decrease and the recovery of the post-exercise FEV_1[24]. In the present study, the AAC_{0-30} was significantly higher in obese asthmatics in comparison with non-obese asthmatics (455.0 *versus* 214.0%, p=0.03).

In spite of the limitations of our sample, these results suggest that there is a different EIB pattern between obese and non-obese asthmatics, revealing that in addition to the higher intensity of the EIB crisis, obese asthmatic individuals may have difficulty to recover normal pulmonary function after physical exercise.

In short, we found that overweight did not increase the EIB frequency in obese asthmatic adolescents compared to non-obese adolescents; however, overweight in asthmatics had a significant influence on the increase in the intensity of and recovery time from the EIB crisis. There is need of further studies involving a larger number of subjects and using the same EIB parameters for obese and non-obese asthmatics, as well as studies assessing the effects of weight loss on the intensity of and recovery time from EIB in obese asthmatics.

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