

Respiratory muscle strength in children and adolescents with asthma: similar to that of healthy subjects?*

Força dos músculos respiratórios em crianças e adolescentes com asma:
similar à de indivíduos saudáveis?

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Abstract

Objective: To compare children/adolescents with mild or moderate asthma and healthy subjects in terms of respiratory muscle strength, correlating it with spirometric variables in the former group. **Methods:** This was a cross-sectional study involving individuals 6-16 years of age and clinically diagnosed with mild/moderate asthma, together with a group of healthy, age- and gender-matched subjects. We determined spirometric values, as well as MIP and MEP, and we selected three reproducible measurements (variation < 10%). **Results:** We evaluated 75 patients with asthma and 90 controls. The mean age was 10.0 ± 2.6 years. There were no statistically significant differences between the controls and the asthma group regarding MIP (-89.7 ± 26.7 cmH₂O vs. -92.2 ± 26.3 cmH₂O; $p = 0.541$) or MEP (79.2 ± 22.9 cmH₂O vs. 86.4 ± 24.0 cmH₂O; $p = 0.256$). The groups were subdivided by age (children and adolescents: 6-12 and 13-16 years of age, respectively). Within the asthma group, there was a significant difference between the child and adolescent subgroups in terms of MEP (74.1 ± 24.1 cmH₂O vs. 92.1 ± 21.9 cmH₂O; $p < 0.001$) but not MIP ($p = 0.285$). Within the control group, there were significant differences between the child and adolescent subgroups in terms of MIP (-79.1 ± 17.7 cmH₂O vs. -100.9 ± 28.1 cmH₂O; $p < 0.001$) and MEP (73.9 ± 18.7 cmH₂O vs. 90.9 ± 28.1 cmH₂O; $p < 0.001$). In the asthma group, spirometric variables did not correlate with MIP or MEP. **Conclusions:** In our sample, asthma was found to have no significant effect on respiratory muscle strength.

Keywords: Asthma; Respiratory muscles; Respiratory function tests.

Resumo

Objetivo: Comparar a força dos músculos respiratórios de crianças e adolescentes com asma leve/moderada com a de indivíduos saudáveis e correlacionar variáveis da espirometria com a força desses músculos nos indivíduos com asma. **Métodos:** Estudo transversal com indivíduos (6-16 anos de idade) com diagnóstico clínico de asma leve/moderada e voluntários saudáveis pareados por idade e gênero. Foram determinados valores espirométricos, P_lmáx e P_Emáx, sendo selecionadas três medidas reprodutíveis (variação < 10%). **Resultados:** Foram avaliados 75 pacientes com asma e 90 controles. A média de idade foi de $10,0 \pm 2,6$ anos. Não houve diferenças estatisticamente significantes entre o grupo controle e asma em relação a P_lmáx ($-89,7 \pm 26,7$ cmH₂O vs. $-92,2 \pm 26,3$ cmH₂O; $p = 0,541$) e P_Emáx ($79,2 \pm 22,9$ cmH₂O vs. $86,4 \pm 24,0$ cmH₂O; $p = 0,256$). Os dois grupos foram subdivididos em crianças (6-12 anos) e adolescentes (13-16 anos). Nos subgrupos de crianças e adolescentes no grupo asma, houve diferença da P_Emáx ($74,1 \pm 24,1$ cmH₂O vs. $92,1 \pm 21,9$ cmH₂O; $p < 0,001$), mas não da P_lmáx ($p = 0,285$). Nos subgrupos de crianças e adolescentes no grupo controle, houve diferenças de P_lmáx ($-79,1 \pm 17,7$ cmH₂O vs. $-100,9 \pm 28,1$ cmH₂O; $p < 0,001$) e P_Emáx ($73,9 \pm 18,7$ cmH₂O vs. $90,9 \pm 28,1$ cmH₂O; $p < 0,001$). Não houve correlação das variáveis de espirometria com P_lmáx e P_Emáx nos pacientes do grupo asma. **Conclusões:** Na presente amostra, a presença de asma não determinou alterações significativas na força dos músculos respiratórios.

Descritores: Asma; Músculos respiratórios; Testes de função respiratória.

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Introduction

Asthma is the most common chronic lung disease in children,⁽¹⁻⁴⁾ being characterized by increased airway resistance and air trapping due to reduced expiratory flow. These two factors lead to lung hyperinflation, changing respiratory mechanics and, consequently, impairing kinetics in respiratory muscles.⁽⁵⁾

In patients with obstructive pulmonary disease, the respiratory muscles, especially the inspiratory muscles, are shortened, and this compromises their capacity to generate force.⁽⁶⁻⁸⁾ However, because the respiratory muscles are often subjected to high loads, they might undergo adaptations, including hypertrophy.⁽⁹⁾ This mechanism can act as involuntary muscle training, possibly leading to an increase in strength.^(10,11) Previous studies have shown that this overload causes an increase in oxidative, fatigue-resistant muscle fibers, as well as an increase in the respective myosin molecules, a reduction in sarcomere length, an increase in mitochondrial density, and an increase in capillary density in the diaphragm and intercostal muscles.^(12,13)

Respiratory muscle strength can be measured noninvasively by determining maximal respiratory pressures with a manometer.⁽¹⁴⁾ These pressures reflect not only the strength of respiratory muscle contraction but also the elastic recoil of the chest wall and lungs. While MIP measures the strength of inspiratory muscle contraction, MEP measures expiratory muscle strength.^(15,16)

Previous studies have shown that the variation of MIP among individuals reflects the variation of the structural attributes of the inspiratory muscles, in particular the muscular cross-sectional area of the diaphragm,⁽¹⁷⁻¹⁹⁾ and that adults with asthma have reductions of up to 30% in maximal respiratory pressures as a result of the effects of hyperinflation.⁽²⁰⁾ Measurement of maximal respiratory pressures is very well known and also widely used to assess children with chronic lung disease; however, there are questions about the value of respiratory muscle strength in this group of patients.⁽²¹⁾

The objective of the present study was to compare children/adolescents with mild or moderate asthma and healthy controls in terms of respiratory muscle strength—as determined by measuring maximal respiratory pressures—and correlate MIP and MEP with spirometric variables in the former group.

Methods

This was a cross-sectional study of a probability sample of children and adolescents aged 6-16 years living in the city of Maceió, Brazil, and treated at the Asthma Program Outpatient Clinic, located in the same city. The study was approved by the Research Ethics Committee of the Federal University of São Paulo, located in the city of São Paulo, Brazil. The parents or legal guardians of all participants gave written informed consent.

Two groups were formed, namely asthma and control. The patients in the asthma group had been clinically diagnosed with asthma at least six months prior, in accordance with the Global Initiative for Asthma criteria.⁽²²⁾ All of them were classified as having mild or moderate persistent asthma after having been evaluated by a specialist. The individuals in the control group were matched for age and gender with those in the asthma group and were recruited from two primary health care clinics of the municipal health system during routine visits or visits for immunization.

The exclusion criteria for the two groups were as follows: being under treatment with systemic corticosteroids; having undergone thoracic surgery; having been diagnosed with heart disease or neuromuscular disease; having had upper or lower airway infection in the two weeks preceding the tests; receiving respiratory therapy or any physical training more than twice a week; being unable to perform the pulmonary function test in accordance with the recommendations⁽²³⁾; and having nutritional disorders.⁽²⁴⁾

The study participants in the asthma and control groups were subdivided by age into children (6-12 years of age) and adolescents (13-16 years of age) in order to determine the influence of age (Figure 1).

After admission, each individual was evaluated at a single time point, always in the afternoon. They underwent anthropometric measurement, spirometry, and assessment of respiratory

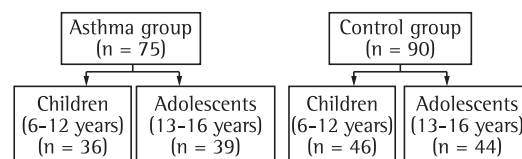


Figure 1 – Groups studied.

muscle strength. All tests and measurements were performed by the same researcher. The individuals evaluated were previously instructed to wear light clothing and not to eat 30 min before the tests. They were also instructed to avoid vigorous physical activity and not to drink alcoholic beverages, coffee, or soft drinks in the 24 h preceding the tests.

Spirometry was performed with an EasyOne-2010® spirometer (NDD Medizintechnik AG, Munich, Germany), which was calibrated daily in accordance with the recommendations of one study.⁽²³⁾ The test was performed in accordance with the aforementioned recommendations,⁽²³⁾ and FVC, FEV₁, FEV₁/FVC, and PEF were measured. The values obtained are expressed as percentage of predicted normal for gender and height.⁽²³⁾

Albuterol (400 µg/dose) was used only for the asthma group, and spirometry was repeated 15 min later. A positive bronchodilator response was defined as an increase ≥ 200 mL or of 12% in FEV₁ or FVC in relation to the baseline values, or a 7% increase in FEV₁ or FVC in relation to the predicted values. This constituted a criterion to confirm the diagnosis of asthma.

An analog manometer (Gerar, São Paulo, Brazil) with an operating range of ± 300 cmH₂O was used to measure MIP and MEP. In accordance with the recommendations of two studies,^(25,26) MEP was measured at TLC (maximal inspiratory maneuver) and MIP was measured at RV (maximal expiratory maneuver). The maneuvers were performed five to eight times or until the last measured value was lower than the second from last. The values should have a maximum variation of 10%, three reproducible curves being required. The highest pressure peaks were recorded, provided that they lasted at least 1 s.

A rigid plastic mouthpiece with an air outlet of 2 mm in diameter distal to the patient was used in order to avoid the influence of the pressures generated by the facial muscles. In addition, the participants were instructed to press their cheeks with their hands during MEP measurement. The accuracy of MIP and MEP measurements was ± 5 cmH₂O. All measurements were performed with the patients in a sitting position.

A 15% difference in inspiratory muscle strength was considered to be a clinically significant value, and the sample size was calculated considering this difference in MIP between the two groups, with a power of 80% and a level of significance of

5%. Therefore, it was estimated that 70 children were required in each group.

Sample homogeneity was confirmed by the Kolmogorov-Smirnov test, and parametric tests were used to compare variables between the groups. Data are expressed as mean and standard deviation.

The primary variables were MIP and MEP, which were compared between the two groups, and the secondary variables were age, gender, and spirometric variables.

The unpaired Student's t-test was used for the comparison of MIP and MEP between the asthma and control groups, as well as between their subgroups (children and adolescents). The same was done for the comparison of FVC, FEV₁, FEV₁/FVC, and age between the groups.

In order to determine the correlation between respiratory muscle strength variables (i.e., MIP and MEP) and spirometric variables (i.e., FEV₁, FVC, and FEV₁/FVC) in the asthma group, we calculated Pearson's correlation coefficient.

For all tests, the level of significance required to reject the null hypothesis was set at 5%.

Results

We evaluated 217 children and adolescents; of those, 165 were included in the study: 75 patients with asthma and 90 controls (Figure 1). There were 41 males (54%) in the asthma group and 43 males (47%) in the control group. Table 1 shows some characteristics of the population studied.

There were no statistically significant differences between the control group and the asthma group regarding MIP (-89.7 ± 26.7 cmH₂O vs. -92.2 ± 26.3 cmH₂O; Figure 2A) or MEP (79.2 ± 22.9 cmH₂O vs. 86.4 ± 24.0 cmH₂O; Figure 2B).

There were no differences in MIP or MEP between males and females in the control group or in the asthma group ($p > 0.05$).

The groups were subdivided by age (children and adolescents). The asthma group comprised 36 children and 39 adolescents, and the control group comprised 46 children and 44 adolescents.

In the control group, MIP and MEP were higher in the adolescents than in the children ($p < 0.001$).

In the asthma group, only MEP was higher in the adolescents than in the children ($p < 0.001$; Table 2).

Table 1 - Characteristics of the population studied.^a

Characteristic	Asthma group	Control group	p*
	(n = 75)	(n = 90)	
Age, years	10.0 ± 2.6	10.0 ± 2.7	0.927
FEV ₁ , % of predicted	76.4 ± 17.5	95.5 ± 10.3	0.001
FVC, % of predicted	96.1 ± 18.6	96.8 ± 17.9	0.852
FEV ₁ /FVC, %	70.4 ± 18.6	85.4 ± 5.7	< 0.001
PEF, mL/s	66.6 ± 19.1	92.4 ± 16.5	0.036

^aValues expressed as mean ± SD. *Student's t-test.

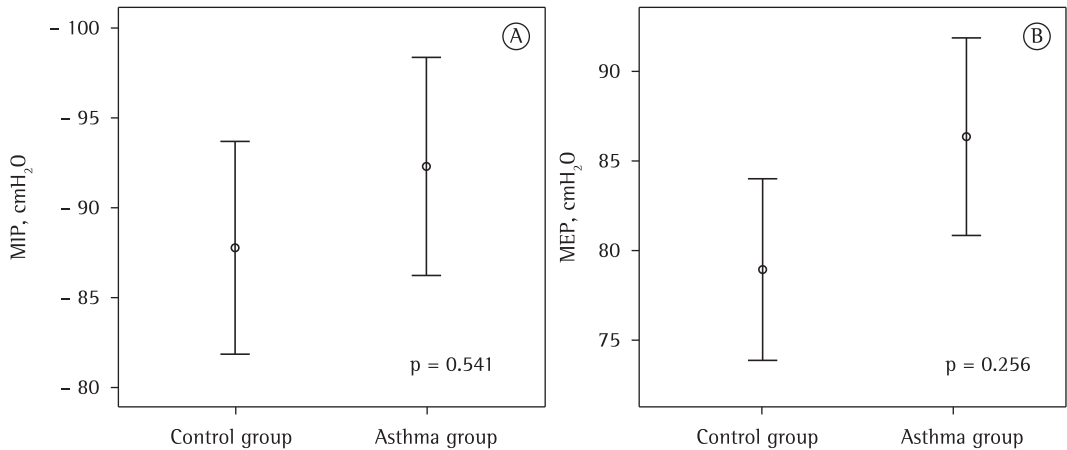


Figure 2 - Error bar chart of maximal respiratory pressures in the groups studied. In A, MIP. In B, MEP.

There were no significant differences between the children with asthma and the control children regarding MIP ($p = 0.117$) or MEP ($p = 0.961$). There were no significant differences in MIP or MEP between the adolescents with asthma and the control adolescents ($p = 0.257$ and $p = 0.291$, respectively).

There were no significant correlations of FEV₁, FVC, or FEV₁/FVC with MIP or MEP ($p > 0.05$; $r < 0.2$ for all).

Discussion

Maximal respiratory pressures reflect respiratory muscle strength. Measurement of these pressures is a simple, reproducible, and noninvasive test that is easy to understand and allows the determination of respiratory muscle weakness and the monitoring of patients with chronic lung disease.^(27,28)

We found no differences in respiratory muscle strength (MIP and MEP) between children with asthma and age- and gender-matched controls or between adolescents with asthma and age- and gender-matched controls. Although the asthma

patients had airflow obstruction, as evidenced by a significant reduction in FEV₁, they showed no impairment of respiratory muscle strength, a finding that is consistent with those of other studies.^(29,30)

Asthma patients with mild or moderate obstructive pulmonary disease might not have significant lung hyperinflation resulting in changes in diaphragm position. Lung hyperinflation increases functional residual capacity, and this leads to changes in respiratory mechanics and flattening of the diaphragm. The flattening of the diaphragm constitutes a mechanical disadvantage, which can be inferred by the reduction in respiratory muscle strength. The patients evaluated in the present study had mild or moderate airway obstruction, which probably explains the similarity in MIP and MEP between the asthma patients and the healthy subjects.

Among the patients with asthma, MEP was significantly lower in the children than in the adolescents, which was expected because of the physiological growth. Wagener et al.⁽¹⁶⁾ found that respiratory muscle strength was higher in post-

Table 2 – MIP and MEP in the groups and subgroups studied.^{a,b}

Pressure	Asthma group		p*	Control group		p*
	Children	Adolescents		Children	Adolescents	
MIP, cmH ₂ O	-87.5 ± 26.0	-94.5 ± 26.4	0.285	-79.1 ± 17.7	-100.9 ± 28.1	< 0.001
MEP, cmH ₂ O	74.1 ± 24.1	92.1 ± 21.9	< 0.001	73.9 ± 18.7	90.9 ± 28.1	< 0.001

^aValues expressed as mean ± SD. ^bChildren: 6-12 years of age; adolescents: 13-16 years of age. *Student's t-test.

pubertal individuals and that MEP was lower in children than in adolescents or adults, a finding that is consistent with those of the present study. Those results were explained by the greater muscle area in the older individuals. We believe that growth and pubertal stage influence respiratory muscle strength, as they are known to influence upper and lower body muscle strength. We did not assess the pubertal stage of the participants; the groups were subdivided exclusively on the basis of chronological age, which prevents us from drawing definitive conclusions regarding this issue, although changes in respiratory muscle strength have been reported to correlate with age.⁽²⁷⁾

In the asthma group, MIP was similar between the children and adolescents. Having in mind muscle growth and development, we expected that inspiratory muscle strength would behave similarly to expiratory muscle strength, i.e., greater age would translate to higher values. However, this proved not to be the case.

Growth-related variations in MIP have been described by various authors.^(16,17,25) However, Galtier et al. found that MIP only partially reflected the development of respiratory muscle strength, given that respiratory muscle strength is the product of pressure and surface area over which pressure is applied and that both increase with growth.⁽²⁵⁾ Those authors measured maximal respiratory pressures in healthy children aged 8-11 years and correlated the pressures with lung volumes and chest wall diameters. They concluded that, as in adults, MIP in children varies with lung volumes, being directly related to VC and increasing with age, even before puberty; therefore, greater age and higher VC translate to higher MIP.⁽²⁵⁾ On the basis of the same principle, Weiner et al.⁽²⁹⁾ assessed the effects of lung hyperinflation on respiratory muscle function in patients with asthma. Those authors found that only male patients with asthma had reduced respiratory muscle strength and efficiency, there being no correlation between age and reduced respiratory

muscle strength or efficiency. Therefore, although lung hyperinflation can lead to changes in MIP, age has no direct influence on MIP.

Our finding that MIP was similar between the children and adolescents in the asthma group but not between those in the control group allows us to infer that the pulmonary function impairment caused by the disease can prematurely affect respiratory muscle strength in children, making it similar to that of adolescents. This finding has been reported by other authors⁽¹⁰⁻¹²⁾ as being a type of involuntary muscle training caused by airway closure leading to changes in MIP in individuals with obstructive pulmonary disease. Children with increased MIP will not present with impaired respiratory mechanics at this point, because the respiratory system is still developing and can adapt. However, knowing that this is probably due to airway obstruction and that asthma chronicity is associated with the completion of respiratory system development, flattening of the diaphragm resulting from hyperinflation can produce greater or lesser impairment of MIP.

Assuming that airway obstruction would cause an increase in MIP, we expected that maximal respiratory pressures in patients with asthma would correlate with spirometric variables, as described in previous studies.^(15,18,30) However, in our study, neither MIP nor MEP correlated with FEV₁, FVC, or FEV₁/FVC in the asthma group. This finding is inconsistent with the literature and can be explained by the degree of airway obstruction in the group of patients under study. The patients evaluated in the present study had mild or moderate obstruction, which probably contributed to the lack of significant correlation between spirometry results and respiratory muscle strength. Although we found no significant correlations, we found changes in MIP, meaning that the degree of obstruction was probably sufficient to cause an early increase in MIP in the children with asthma.

The results of the present study cannot be generalized to patients with severe asthma, because such patients were not included in the study protocol. We believe that there is a need for specific studies of patients with severe asthma, and we can infer that there are changes in respiratory muscle strength in this group of patients. However, a study protocol including a specific methodology should be developed to address this issue.

In conclusion, mild or moderate persistent asthma was found to have no significant effect on respiratory muscle strength. In the control group, MIP and MEP were found to be lower in the children than in the adolescents, whereas, in the asthma group, MIP was similar between the children and adolescents, meaning that MIP was prematurely increased in the children. There were no significant correlations between spirometric variables and maximal respiratory pressures.

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