

Aerobic capacity and skeletal muscle function in children with asthma

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ABSTRACT

Background Peripheral muscle strength and endurance are decreased in patients with chronic pulmonary diseases and seem to contribute to patients' exercise intolerance. However, the authors are not aware of any studies evaluating peripheral muscle function in children with asthma. It seems to be implied that children with asthma have lower aerobic fitness, but there are limited studies comparing the aerobic capacity of children with and without asthma. The present study aimed to evaluate muscle strength and endurance in children with persistent asthma and their association with aerobic capacity and inhaled corticosteroid consumption.

Methods Forty children with mild persistent asthma (MPA) or severe persistent asthma (SPA) (N=20 each) and 20 children without asthma (control group) were evaluated. Upper (pectoralis and latissimus dorsi) and lower (quadriceps) muscle strength and endurance were assessed, and cardiopulmonary exercise testing was performed. Inhaled corticosteroid consumption during the last 6 and 24 months was also quantified.

Results Children with SPA presented a reduction in peak oxygen consumption (VO_2) (28.2 ± 8.1 vs 34.7 ± 6.9 ml/kg/min; $p < 0.01$) and quadriceps endurance (43.1 ± 6.7 vs 80.9 ± 11.9 repetitions; $p < 0.05$) compared with the control group, but not the MPA group (31.5 ± 6.1 ml/kg/min and 56.7 ± 47.7 repetitions respectively; $p > 0.05$). Maximal upper and lower muscle strength was preserved in children with both mild and severe asthma ($p > 0.05$). Finally, the authors observed that lower muscle endurance weakness was not associated with reductions in either peak VO_2 ($r = -0.22$, $p > 0.05$) or corticosteroid consumption ($r = -0.31$, $p > 0.05$) in children with asthma.

Conclusion The findings suggest that cardiopulmonary exercise and lower limb muscle endurance should be a priority during physical training programs for children with severe asthma.

INTRODUCTION

Asthma is a chronic inflammatory disorder of the airways that is characterised by recurring episodes of wheezing, breathlessness, chest tightness and coughing, particularly during the night or in the early morning.¹ Although many factors may trigger dyspnoea (shortness of breath) in patients with asthma, exercise is one of the most prevalent causes; it induces increases in airway resistance in 50–90% of patients.² The fear of experiencing an episode of breathlessness prevents many patients, especially those with more severe disease, from taking part in regular play or sports with their peers.³

What is already known on this topic

- It remains unknown if children with asthma have reduced aerobic exercise capacity.
- Evidence shows that patients with chronic respiratory disorders present with peripheral muscle weakness; however it remains unknown if this also applies to patients with asthma.

What this study adds

- Reduced aerobic exercise capacity was observed only in patients with severe persistent asthma, showing that physical limitation is related to disease severity.
- Children with severe persistent asthma have lower limb muscle weakness but not maximal muscle strength.

Physical restrictions caused by asthma symptoms affect patients' quality of life^{4 5} and lead to postural changes⁶ and a sedentary lifestyle.³ On this basis, patients with asthma have been encouraged to participate in regular physical training programs⁷ and many benefits have been observed, such as increase in aerobic capacity, improvement in health-related quality of life, and reduction in breathlessness, daily doses of inhaled corticosteroids and exercise-induced bronchoconstriction.^{8 9} Since aerobic training is the only type of exercise that has been recommended for patients with asthma, it is feasible to suppose that they have a reduced exercise capacity. However, only few studies have compared the peak oxygen consumption (VO_2) in children with and without asthma.¹⁰ In addition, peripheral muscle strength or resistance training or capacity have not been evaluated in patients with asthma.

Peripheral muscle weakness seems to contribute to exercise limitation in patients with chronic respiratory disorders, such as chronic obstructive pulmonary disease (COPD),¹¹ cystic fibrosis^{12 13} and idiopathic pulmonary fibrosis.¹⁴ In patients with COPD, a decrease in muscle skeletal mass has been associated with many factors, including hypoxemia,¹⁵ malnutrition,¹⁶ lower aerobic capacity,¹⁷ chronic airway obstruction¹⁸ and corticosteroid consumption.¹⁹

Because patients with persistent asthma have some clinical similarities to patients with COPD, such as lower exercise capacity,²⁰ airway obstruction¹ and clinical treatment based on corticosteroids,¹ the authors' hypothesis is that children with severe asthma also have muscle weakness. In addition, a better understanding of the distribution and causes of muscle weakness in patients with asthma would help to develop new therapeutic approaches in rehabilitation programs for these patients. Thus, the main goal of the present study was to evaluate peripheral muscle strength and endurance in children with severe persistent asthma and to evaluate the possible relationship between peripheral muscle function and aerobic capacity or corticosteroid consumption.

METHODS

Participants and study design

Forty children with mild persistent asthma (MPA) or severe persistent asthma (SPA) (N=20 each) and 20 children without asthma (control group), aged 8–15 years, were evaluated. Children with asthma were recruited from a Tertiary University Hospital specialising in paediatric allergy and asthma. Asthma diagnosis, severity and treatment were established according to the Global Initiative for Asthma guidelines¹ and children were under medical treatment for at least 6 months and considered clinically stable (no crises or changes in medication for at least 90 days). Children with other pulmonary diseases and/or musculoskeletal diseases were excluded. All groups were matched for age, weight, height and pubertal stage.²¹ Asthma and allergic rhinitis were discarded in the control group using the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire (response negative to question 2 'Have you/your child had wheezing or whistling in the chest in the last 12 months?' and total score <6).^{22–23} No children from any of the three groups were involved in any regular exercise training program besides physical gym at school. The study was approved by the Hospital Ethics Committee (protocol 099/06), and patients were enrolled after parents or guardians signed a written informed consent. No remuneration was offered.

After study inclusion, tests were performed on 2 days ranging from 1 to 2 weeks apart. On the first day, children performed spirometry and cardiopulmonary exercise testing, while peripheral muscle strength and endurance tests were performed on the second day.

Measurements

Spirometry was performed before and after inhalation of 400 µg of salbutamol (SensorMedics 229; SensorMedics, Yorba Linda, California, USA), and technical procedures and reproducibility criteria were those recommended by the American Thoracic Society (2005).²⁴ Forced vital capacity (FVC), forced expiratory volume in 1 s (FEV₁) and FEV₁/FVC were measured. Predicted normal values were those proposed by NHANES III.²⁵

Cardiopulmonary exercise testing was performed after spirometry if FEV₁ was greater than 75% of the predicted value. An exercise test was performed using a cycle ergometer (SensorMedics 2000) connected to a computer-based ergospirometer device with breath-by-breath analysis of metabolic, ventilatory and cardiovascular variables. The following data were obtained: oxygen uptake (VO₂ (ml/min), standard temperature, pressure and dry conditions), minute ventilation (VE (litre/min), BTPS) and heart rate. The work

rate was continuously increased in a linear ramp pattern (15 W/min for height <150 cm; 20 W/min for height >150 cm) to provide exercise duration of more than 8 min and less than 12 min.²⁶ The children began by cycling at unloaded work rate with a minimum of 3 min during a warm-up phase. They were then instructed to maintain a constant pedalling rate between 50 and 70 rpm. The predicted VO₂max was calculated according to the equations proposed for children by Cooper and coworkers²⁷ (VO₂max = 28.5×weight+288.2).

Peripheral muscle strength and endurance measurements were performed with leverage weight machines (Biodelta, São Paulo, Brazil), and children performed three exercises involving the lower limb muscle (extending from the gluteus to the foot, including the buttocks, hip and leg), evaluated by the leg-press exercise (mostly quadriceps muscle) and the upper limb muscle (extending from the deltoid to the hand, including the arm, axillar and shoulder), tested by the seated chest press (mostly pectoralis major muscles) and seated row (mostly latissimus dorsi muscles) exercises. Before testing, all children participated in one training session to learn how to perform the exercises properly. A warm-up session consisting of 10–15 repetitions with no weight and 5 repetitions with a light weight (10 kg for lower muscle groups and 2.5 kg for upper muscle groups) was performed before each testing exercise as previously described.²⁸

Muscle strength was assessed through the determination of one-repetition maximum lifting weight test (1RM).^{28–29} During the 1RM test, the lifted weight was increased until the child attained the maximal load, as previously described.³⁰ The load increment was approximately from 2.5 to 5.0 kg for upper muscle groups and from 10 to 20 kg for lower muscle groups. At least 2 min of rest was given between each effort and the maximal value was the maximum load that the child could lift through the full range of motion.³¹

After establishing maximal strength force (1RM test) for each exercise, a muscle endurance test was performed by a single set of continuous repetitions with a 50% load of 1RM until exhaustion. The task was discontinued when the child was unable to achieve a full range of motion or chose to stop volitionally. Muscle endurance was defined as the number of repetitions.³²

Inhaled corticosteroid use was calculated from the average daily dose taken during the previous 6 and 24 months. All doses were converted to the drug with the highest prevalence of use in the sample (budesonide). This assessment was based on determination of clinical potency when comparing inhalatory corticosteroid doses: flunisolide = triamcinolone (0.33) < beclomethasone (0.60) < budesonide (0.98) < fluticasone (1.20).¹

STATISTICAL ANALYSIS

The sample size of 60 children was calculated taking into consideration an increase in the maximal muscle strength of 10%, a SD of 15% using the analysis of variance (ANOVA) with three groups (controls, MPA and SPA) and a power of 80%. The Kolmogorov–Smirnov test was used to check for normal distribution of data. The one-way ANOVA was used to compare absolute values among studied groups followed by the Tukey post hoc test. Linear association analysis was performed using the Pearson correlation test. For all tests, a p value of less than 5% was considered statistically significant (p<0.05). All procedures were calculated using a statistical software package (SigmaStat, version 3.11; San Juan, CA, USA).

RESULTS

All three groups presented similar anthropometric characteristics (table 1). The length of time with disease did not differ between the SPA and the MPA groups (table 1). However, the SPA group used a higher daily dose of inhaled steroids over the previous 6 months than the MPA group ($p<0.001$; table 1). As expected, the control group had higher FEV_1/FVC values than the SPA and MPA groups ($p<0.001$; table 1).

Children with SPA had lower maximal aerobic capacity (peak VO_2) compared with the control group (28.2 ± 8.1 and 34.7 ± 6.9 ml/kg/min, respectively; $p=0.02$; figure 1), and 55% of the SPA group presented peak VO_2 values $<70\%$, while this value was only 15% in the control group. The MPA group did not present a difference in peak VO_2 when compared with either the SPA or control groups. In addition, the SPA group presented lower values of O_2 pulse and reached an anaerobic threshold at higher levels compared with the control group (table 1). In contrast, children presented similar levels of perceived fatigue and dyspnoea.

No difference in muscle strength was observed among the three groups in any of the exercises performed (quadriceps, pectoralis major and latissimus dorsi muscles) (figure 2A). The quadriceps muscle endurance was reduced in the SPA group compared with the control group (43.1 ± 6.7 vs 80.9 ± 11.9 repetitions, respectively; $p=0.04$) but not compared with the MPA group ($p=0.17$; figure 2B). However, there was no difference in the muscle endurance of the pectoralis major ($p=0.82$) or latissimus dorsi muscles ($p=0.06$) among the three studied groups.

The linear relationship between aerobic capacity and muscle strength was also evaluated in children with mild and severe asthma, and a stronger association between peak VO_2 with either pectoralis or latissimus dorsi muscle strength was observed (table 2). In addition, a weaker relationship was found between quadriceps muscle strength and aerobic capacity in children with asthma. Interestingly, no significant linear relationship was observed between muscle endurance (quadriceps, pectoralis major or latissimus dorsi muscle) and peak VO_2 in children with asthma (table 2).

The daily dose of inhaled steroids over the last 6 and 24 months was not related to either muscle strength or endurance in children with asthma (table 3). An association between systemic corticosteroid consumption and muscle strength was investigated; however, because few children used this steroid (four in the SPA group and two in the MPA group), no relationship was observed.

DISCUSSION

The present study shows that children with SPA have a decreased maximal aerobic capacity and quadriceps muscle endurance but do not have differences in upper or lower limb muscle strength compared with the control group. In addition, the amount of inhaled corticosteroid consumption does not seem to be involved in either muscle strength function or in the reduction of quadriceps muscle endurance. These results show that aerobic conditions and quadriceps endurance should be a priority in exercise training programs for children with asthma independent of corticosteroid consumption.

Table 1 Anthropometric, pulmonary function and clinical data

	Control (N=20)	MPA (N=20)	SPA (N=20)	p Value
Anthropometric				
Age (years)	11.2 $\pm$ 1.8	10.5 $\pm$ 2.1	10.9 $\pm$ 1.9	0.58
Weight (kg)	43.3 $\pm$ 10.8	39.6 $\pm$ 10.5	39.5 $\pm$ 9.2	0.40
Height (cm)	148.5 $\pm$ 11.4	144.9 $\pm$ 10.8	143.6 $\pm$ 6.3	0.28
BMI (kg/m ²)	19.4 $\pm$ 3.5	18.5 $\pm$ 2.7	19.0 $\pm$ 3.8	0.67
Pulmonary function				
FVC (litre)	2.73 $\pm$ 0.7	2.55 $\pm$ 0.6	2.34 $\pm$ 0.3	0.13
(% pred)	95.7 $\pm$ 9.9	96.2 $\pm$ 14.3	90.5 $\pm$ 15.4	0.33
FEV ₁ (litre)	2.46 $\pm$ 0.6	2.18 $\pm$ 0.5	1.88 $\pm$ 0.3*	0.004
(% pred)	94.7 $\pm$ 9.6	89.5 $\pm$ 11.3	86.4 $\pm$ 11.2*	0.05
FEV ₁ /FVC	90.4 $\pm$ 4.0	85.2 $\pm$ 6.0	80.2 $\pm$ 7.2	<0.001
Asthma				
Asthma diagnosis (years)	0 $\pm$ 0	8.1 $\pm$ 2.7*	9.0 $\pm$ 2.2*	<0.001
Budesonide—6 months (μ g/day)	0 $\pm$ 0	180 $\pm$ 222	782 $\pm$ 149	<0.001
Budesonide—2 years (μ g/day)	0 $\pm$ 0	234 $\pm$ 284	757 $\pm$ 157	<0.001
Aerobic capacity				
VO_2 peak (ml O_2 /kg/min)	34.7 $\pm$ 6.9	31.6 $\pm$ 6.1	28.2 $\pm$ 8.1*	0.02
VO_2 peak (% pred)	85.0 $\pm$ 13.6	79.0 $\pm$ 11.7	69.2 $\pm$ 15.7*	0.003
VO_2 /HR peak (ml O_2 /kg/bpm)	7.8 $\pm$ 2.4	6.7 $\pm$ 1.6	6.2 $\pm$ 2.0†	0.04
VO_2 AT (% peak)	42.8 $\pm$ 7.5	46.4 $\pm$ 9.4	51.1 $\pm$ 10.6†	0.04
Ventilatory reserve	75.0 $\pm$ 13.0	75.0 $\pm$ 20	66.0 $\pm$ 12	0.13
Muscle fatigue (Borg scale)	5.6 $\pm$ 2.6	6.3 $\pm$ 2.4	5.0 $\pm$ 2.8	0.32
Dyspnoea (Borg scale)	4.6 $\pm$ 4.2	4.2 $\pm$ 2.5	3.8 $\pm$ 2.8	0.78

Data are presented as the mean $\pm$ SD. Statistical analysis among all groups was performed using analysis of variance (ANOVA) with post-hoc Tukey and p values <0.05 were considered significant. Data comparison was performed among controls and patients with mild persistent asthma (MPA) and severe persistent asthma (SPA).

VO_2 /HR = O_2 pulse; cardiac reserve = peak heart rate/max heart rate $\times$ 100; ventilatory reserve = peak ventilation/maximal voluntary ventilation $\times$ 100.

* $p<0.01$ compared with control group.

† $p=0.05$ compared with control group.

AT, anaerobic threshold; BMI, body mass index; FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; HR, heart rate; VO_2 , oxygen consumption.

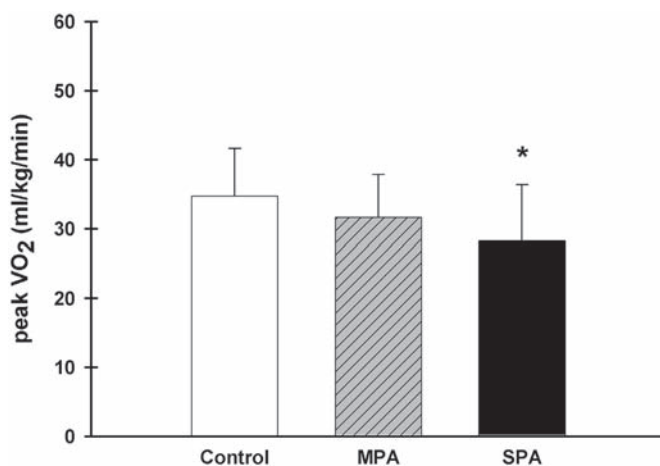


Figure 1 Maximal aerobic capacity of children with and without asthma. Data are presented as the mean±SD. Comparison was performed among all three groups; p values <0.05 were considered significant. *p=0.04 (severe persistent asthma (SPA) vs control group; Tukey test). MPA, mild persistent asthma. VO₂, oxygen consumption.

Exercise training has been widely used as an adjuvant treatment because there is evidence suggesting that it can improve health-related quality of life^{9 33} and reduce dyspnoea,³⁴ exercise induced-bronchoconstriction⁹ and airway inflammation.³³ There is no agreement in the literature about the exercise training for children with asthma, and many distinct programs have been described with distinct exercise modalities.³⁴ Aerobic training is the most commonly used training program for children with asthma; there seems to be an agreement in the literature that these children have a reduced aerobic capacity compared with their peers.⁷ Interestingly, this issue remains controversial because there are few studies comparing peak VO₂ between children with and without asthma. Only two studies have shown that patients with severe persistent asthma have lower maximal aerobic capacity than controls.^{35 36} However, two studies have shown that children with asthma have a similar maximum aerobic capacity compared with children without asthma.^{37 38}

In the present study, aerobic capacity was found to be reduced in children with severe persistent but not mild asthma. Many features can explain the discrepancies observed among this study and other studies, such as the degree of disease severity and bias in patient selection. Santuz and coworkers³⁷ compared controls with patients with asthma (including mild and moderate), while this study evaluated the two disease severities separately. Boas and coworkers³⁸ also suggested that patients with asthma have a similar peak VO₂ compared with those without asthma, but asthma severity was not described. These results suggest that only patients with SPA have a reduction in maximal aerobic capacity, which can be hypothesised to occur because of patients' aerobic deconditioning. Peak VO₂ verified in the healthy control group (34.7 ml/kg/min) can be considered lower if compared with other studies (≈40 ml/kg/min)^{39 40} and a possible explanation is that the Brazilian population has a lower peak VO₂ compared with the North American, European and Japanese populations.^{41 42} Even so, the average peak VO₂ of the controls in this study was inside the range for normality (table 1).²⁷

In this study, the SPA group presented lower peak VO₂ and O₂ pulse, showing the children's physical deconditioning. However, there was no difference in the ventilatory reserve and in the

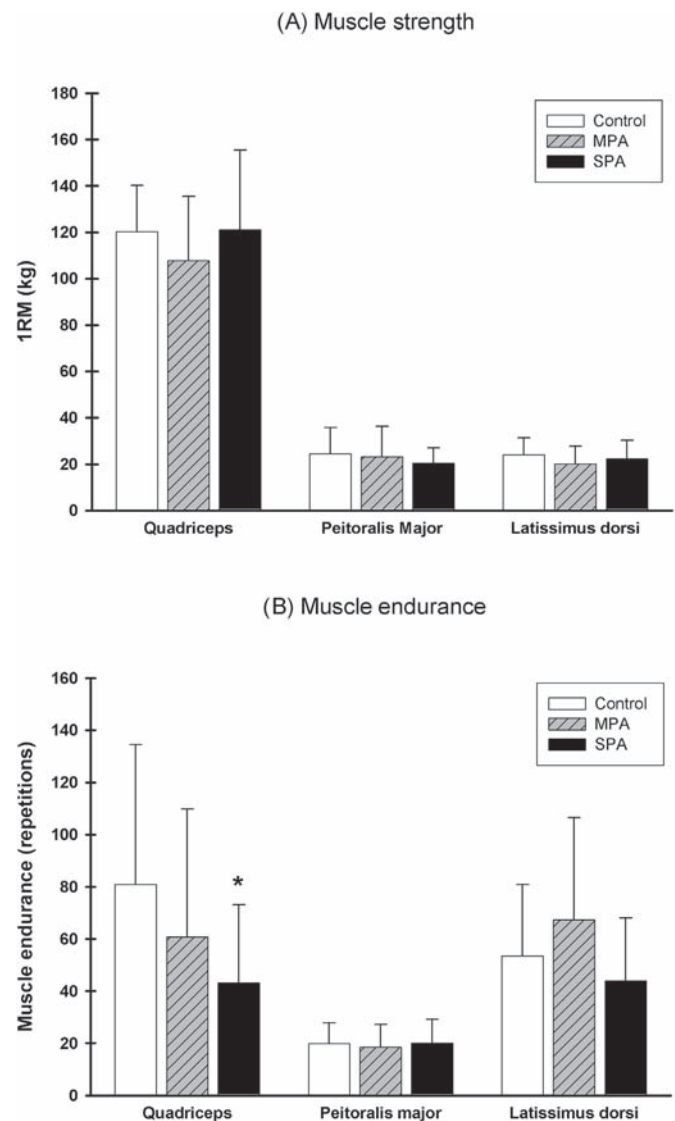


Figure 2 (A) Maximum weight lifted once. (B) Total number of repetitions performed at 50% of maximum weight lifted. Data are presented as the mean±SD. Comparison was performed among all three groups; p values <0.05 were considered significant. Quadriceps=leg-press exercise involving knee and hip muscles extension; pectoralis major=chest-press exercise involving elbow extension, chest and shoulder muscles; latissimus dorsi=row exercise involving elbow flexion, shoulder and back muscles. *p=0.02 (control group vs severe persistent asthma (SPA); Tukey test). 1RM, one-repetition maximum lifting weight test; MPA, mild persistent asthma.

perception of leg fatigue and dyspnoea among all groups, suggesting that maximal effort was attained similarly in children from all groups. The results showing a reduction in O₂ pulse in the SPA group at peak exercise corroborates the previous findings of Varray and colleagues.³⁶ Their hypothesis is that during maximal exercise these patients breathe high tidal volume that leads to a decrease in left ventricular performance.

Previous studies have shown that patients with chronic respiratory diseases, such as COPD,¹¹ cystic fibrosis¹² and idiopathic pulmonary fibrosis,¹⁴ have impaired peripheral muscle strength. Thus, it can be hypothesised that children with asthma could also develop such an impairment. In COPD, the most evaluated muscles are quadriceps, pectoralis major and

Table 2 Linear relationship among muscle strength and endurance with maximal aerobic capacity (peak VO_2)

Strength (kg)	Asthma group (n=40) (mild and severe)		Control group (n=20)	
	R	p Value	R	p Value
Quadriceps	0.34	0.02	-0.29	0.21
Pectoralis major	0.59	<0.001	0.73	<0.001
Latissimus dorsi	0.69	<0.001	0.70	<0.001
Endurance (repetitions)				
Quadriceps	0.22	0.16	0.25	0.28
Pectoralis major	0.29	0.06	0.27	0.23
Latissimus dorsi	0.14	0.38	-0.24	0.29

Linear relationship was analysed in patients with asthma as a group (mild and severe) and control group.
Quadriceps=leg-press exercise; pectoralis major=chest-press exercise; latissimus dorsi=rowing exercise.

Table 3 Linear relationship between muscle performance and inhaled corticosteroid usage

Budesonide (6 months)	Strength		Endurance	
	R	p Value	R	p Value
Quadriceps	0.24	NS	-0.30	NS
Pectoralis major	-0.20	NS	0.02	NS
Latissimus dorsi	0.10	NS	-0.36	NS
Budesonide (2 years)				
Quadriceps	0.12	NS	-0.31	NS
Pectoralis major	-0.35	NS	-0.07	NS
Latissimus dorsi	-0.03	NS	-0.34	NS

Quadriceps=leg-press exercise; pectoralis major=chest-press exercise; latissimus dorsi=row exercise.
NS, non-significant.

latissimus dorsi,¹⁸ and the same muscle groups were studied in this study. Contrary to the authors' hypothesis, muscle strength was preserved in children with either MPA or SPA. There is only one study evaluating peripheral muscle strength in patients with asthma. Only a modest reduction was shown in the inspiratory muscles and no difference in quadriceps strength was observed in adults with asthma.⁴³ Taken together, it seems that muscle strength weakness observed in patients with other respiratory diseases cannot be extrapolated to either adults or children with asthma. Although no differences were observed in the muscle strength of children in this study, further studies should be performed in other patients with asthma, including those with refractory disease¹⁸ and obese patients⁴⁴ who present increased expression of tumour necrosis factor α , a T helper 1 cytokine that may be involved in muscle dysfunction in other respiratory diseases.⁴⁵

This study found that children with SPA presented a reduction in quadriceps muscle but not in upper limb muscle (either pectoralis or latissimus dorsi) endurance. Several factors seem to contribute to muscle dysfunction in patients with chronic respiratory diseases like hypoxemia,¹⁵ malnutrition,¹⁶ corticosteroid treatment¹⁹ and exercise capacity.¹⁷ Because the children in this study did not present cachexia or hypoxemia at rest, the effect of inhaled corticosteroid consumption and a decrease in aerobic capacity on the reduction of quadriceps endurance was evaluated. Interestingly, no association was observed between corticosteroid consumption and a reduction in either muscle endurance or aerobic capacity. In addition, a relationship was not observed between aerobic capacity and peripheral muscle endurance in children with asthma, suggesting that a reduction in both outcomes may not be interrelated. Despite the fact that peripheral muscle weakness was not observed in patients with asthma, a strong relationship was verified between maximal aerobic capacity (peak VO_2) and pectoralis and latissimus

dorsi muscle strength. Although the findings of this study corroborate the findings of Dourado *et al*,⁴⁶ who observed a strong association between exercise capacity and maximal muscle strength in patients with COPD ($r=0.52$; $p<0.01$), the authors do not think that this relationship has any clinical relevance because the controls also presented a similar relationship between upper limb strength and peak VO_2 (table 2).

Study strengths and limitations

This study presents four limitations. First, it included children with a wide age range (from 8 to 15 years old); however, the authors believe that this did not affect the results because participants were age and pubertal stage matched. Second, although all included children reported not participating in any extra activity besides routine school exercise, the level of their daily physical activities was not assessed. Third, muscle strength was measured using the 1RM test instead of isokinetic dynamometry. Although isokinetic equipment can be more sensitive to muscle strength evaluation, the machines are designed for adults, and they are difficult to fit to children, especially younger children. Finally, because the children were not used to performing maximal muscle strength tests, they required a large number of familiarisation sessions to perform the 1RM test.

The results indicate that children with SPA have smaller aerobic capacity and quadriceps muscle endurance but normal muscle strength. This suggests that cardiopulmonary exercise and lower limb muscle endurance should be included in physical training programs for these children.

Competing interests None.

Patient consent Obtained.

Ethical approval This study was conducted with the approval of the Hospital of University of São Paulo Ethics Committee (protocol 099/06).

Provenance and peer review Not commissioned; externally peer reviewed.

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