Children and adolescents with mild intermittent or mild persistent asthma: aerobic capacity between attacks*

Capacidade aeróbica em crianças e adolescentes com asma intermitente e persistente leve no período intercrises

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Abstract

Objective: To assess children and adolescents diagnosed with mild intermittent or mild persistent asthma, in terms of their aerobic capacity between attacks. **Methods:** We included 33 children and adolescents recently diagnosed with asthma (mild intermittent or mild persistent) and 36 healthy children and adolescents. Those with asthma were evaluated between attacks. All participants underwent clinical evaluation; assessment of baseline physical activity level; pre- and post-bronchodilator spirometry; and a maximal exercise test, including determination of maximal voluntary ventilation, maximal oxygen uptake, respiratory quotient, maximal minute ventilation, ventilatory equivalent, ventilatory reserve, maximal HR, SpO_2, and serum lactate. **Results:** No significant differences were found among the groups (intermittent asthma, persistent asthma, and control) regarding anthropometric or spirometric variables. There were no significant differences among the groups regarding the variables studied during the maximal exercise test. **Conclusions:** A diagnosis of mild intermittent/persistent asthma has no effect on the aerobic capacity of children and adolescents between asthma attacks.

Keywords: Asthma; Exercise; Respiratory function tests.

Resumo

Objetivo: Aferir a capacidade aeróbica de crianças e adolescentes com diagnóstico de asma brônquica intermitente leve ou persistente leve no período intercrises. **Métodos:** Foram estudadas 33 crianças e adolescentes com diagnóstico clínico recente de asma leve intermitente e asma leve persistente, no período intercrises, e 36 crianças e adolescentes saudáveis. Foram realizadas avaliação clínica, avaliação do nível basal do nível de atividade física, espirometria antes e após o uso de broncodilatador e determinação de ventilação voluntária máxima, consumo máximo de oxigênio, quociente respiratório, ventilação minuto máxima, equivalente ventilatório, reserva ventilatória, FC máxima, SpO_2 e lactato. **Resultados:** Não foram encontradas diferenças significativas entre os grupos asma intermitente, asma persistente e controle em relação às variáveis antropométricas e espirométricas. Não houve diferenças significativas em relação às variáveis analisadas durante o teste de esforço máximo entre os grupos. **Conclusões:** O diagnóstico de asma intermitente ou persistente leve não influenciou a capacidade aeróbica em crianças e adolescentes no período intercrises.

Descritores: Asma; Exercício; Testes de função respiratória.

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Introduction

Asthma is a chronic inflammatory disease characterized by lower airway hyperresponsiveness and variable airflow limitation that can resolve spontaneously or with treatment; the clinical manifestations of asthma include recurrent episodes of wheezing, dyspnea, chest tightness, and cough, particularly at night and upon waking in the morning.[1] Exercise capacity expresses the temporal state of acute and chronic physiological adaptations in individuals. The temporal component implies that those adaptations have transitory and lasting effects. There is a consensus that, during an attack, asthma patients experience a considerable reduction in exercise capacity, which can be recovered as soon as the attack is controlled. However, because asthma symptoms lead to impaired health-related quality of life, many asthma patients choose to adopt a sedentary lifestyle.[2-4] Although it is commonly believed that children with asthma have reduced aerobic capacity, there are conflicting data in the literature.[5] Although recent studies have suggested that reduced aerobic capacity is related to greater disease severity,[6] the impact of asthma on patients with less severe disease remains unclear.

Because asthma is the most prevalent chronic disease in children and adolescents, because most asthma patients have mild intermittent or mild persistent disease,[1] and because regular physical activity has been proven to have beneficial effects,[7-9] it is essential to determine whether asthma has negative effects on exercise capacity between attacks, the approach to physical training being based on the answer to this question. Therefore, the objective of the present study was to assess children and adolescents with mild intermittent or mild persistent asthma, in terms of their aerobic capacity between attacks.

Methods

We evaluated 33 children and adolescents recently diagnosed with mild intermittent or mild persistent asthma and 36 healthy children and adolescents (control group). All participants were in the 11-14 year age bracket, those with asthma having been evaluated between attacks. None of the asthma patients were receiving inhaled corticosteroid therapy at the time of enrollment. The asthma patients were recruited from among those being treated at the pediatric outpatient clinic of the Santa Maria University Hospital, located in the city of Santa Maria, Brazil. The diagnosis and severity of asthma were established in accordance with the Global Initiative for Asthma criteria.[1] Stable disease was defined as no attacks or medication changes in the last 90 days. We excluded children/adolescents with other respiratory diseases, those with symptoms of viral infection (cold and flu) in the last six weeks, and those with abnormal at-rest pulmonary function test (spirometry) results on the day of the test. We ruled out asthma and allergic rhinitis in the control group by administering the International Study of Asthma and Allergies in Childhood questionnaire,[10,11] a negative answer to question 2 and a total score < 6 indicating the absence of the two diseases. We determined the level of physical activity by administering the International Physical Activity Questionnaire (IPAQ), short version.[12,13] We used the Lohman equation to calculate the percentage of body fat.[14]

The present study was approved by the Research Ethics Committee of the Federal University of Santa Maria Health Sciences Center. The parents or legal guardians of all participants gave written informed consent.

Spirometry was performed with a Vmax Series 229 spirometer (SensorMedics, Yorba Linda, CA, USA) before and after the administration of 400 µg of inhaled albuterol, having been performed in accordance with the acceptability and reproducibility criteria established by the American Thoracic Society[15] and the reference values proposed by Knudson et al.[16] In addition to measuring the spirometric values, we measured maximal voluntary ventilation (MVV), and the volumes were corrected for body temperature, ambient pressure, and saturated air.

Exercise testing was performed on a 10200 ATL treadmill (Inbramed, Porto Alegre, Brazil), in accordance with the protocol proposed by Mader et al.,[17] until maximal voluntary effort was achieved. Twenty minutes before the exercise test, we administered 400 µg of inhaled albuterol with a spacer, in order to prevent exercise-induced bronchospasm. Maximal oxygen uptake (VO_2max), respiratory quotient (RQ), minute ventilation (V_E), and ventilatory equivalent for oxygen (V_E/VO_2) were measured with the abovementioned spirometer (SensorMedics), whereas serum lactate was measured with a glucose/lactate analyzer (model Biosen 5030; EKF Diagnostics, Cardiff, UK). Blood samples were collected at the end of each stage (5 min). We monitored HR with an Accurex Plus™ HR monitor (Polar Electro Ou, Kempele, Finland). All variables were measured at rest, during exercise, and during recovery.

The pulmonary function test and the exercise test were performed in a climate-controlled environment, i.e., at a temperature of 18-26°C and a relative humidity of 55-60%.

The data collected were evaluated for normality by the Shapiro-Wilk test (n < 2,000), and descriptive statistical analysis was performed. The variables age, height, body mass, percentage of body fat, FVC, FEV_1, FEV_1/FVC, PEF, MVV, VO_2max, ventilatory reserve, V_E/VO_2, RQ, and International Study of Asthma and Allergies in Childhood questionnaire score showed normal distribution, ANOVA being therefore used in order to compare the means. The variables that showed statistically significant differences, namely pre-bronchodilator FEV_1 and FEV_1/FVC (both in % of predicted), were analyzed by Duncan's post hoc test. The variables that showed non-normal distribution, namely IPAQ score, running speed, exercise duration, maximal HR, and serum lactate, were analyzed by the Kruskal-Wallis test. All statistical analyses were performed with the program Statistical Analysis System, version 8.2 (SAS Institute, Cary, NC, USA).

Results

The anthropometric characteristics were similar among the three groups studied (mild intermittent asthma, mild persistent asthma, and control), as were the physical activity characteristics. As shown in Table 1, ANOVA showed no statistically significant differences among the groups regarding age, body mass, height, or percentage of body fat; in addition, the Kruskal-Wallis test showed no statistically significant differences among the groups regarding the level of physical activity, as measured by the IPAQ score.

As expected, there were no significant differences among the groups regarding pulmonary function test results (Table 2). Although we found a significant difference among the groups regarding pre-bronchodilator FEV_1/FVC (% of predicted), the means were above 80%, which is considered normal for the age group under study. The results showed no airway obstruction, confirming that the children and adolescents were between attacks. As can be seen in Table 2, there were no significant differences among the groups regarding MVV (in absolute values or in % of predicted). There were no statistically significant differences among the groups regarding the variables analyzed during the maximal cardiopulmonary exercise test, namely maximal V_E ($V_E$max), ventilatory reserve, V_E/VO_2, RQ, maximal HR, VO_2max, serum lactate, maximum speed attained, and exercise duration (Table 3).

Discussion

The objective of the present study was to assess children and adolescents with mild asthma, in terms of their aerobic capacity between attacks. We chose to study patients with mild intermittent or mild persistent asthma because these are the most prevalent forms of the disease.

Although different levels of baseline physical activity can influence the results of studies such as ours, we found no statistically significant differences among the groups in terms of baseline physical activity, as measured by the IPAQ score. The three groups studied were classified as being physically active.[12] The results of the tests performed showed that the physical performance of the individuals in the control group was better than was that of those in the asthma groups. We believe that this was due to higher routine physical activity in the control group, given that the possibility of experiencing attacks during exercise might prevent the asthma patients from engaging in physical activity more often. However, because the IPAQ is not appropriate to determine that and because this is outside the scope of the present study, we cannot draw definitive conclusions.

Obesity is another variable that affects the physical performance of individuals with or without asthma. According to the classification proposed by Lohman,[14] the percentage of body fat in the three groups studied was optimal. Therefore, the results of the present study should be analyzed from the perspective that the individuals studied were physically active and had an adequate percentage of body fat, which was similar among the three groups.

Group homogeneity is important when the objective is to compare individuals with asthma of varying severity and those without in terms of their aerobic capacity. Homogeneity reduces the variability in pulmonary evaluation results. As shown in Table 2, none of the patients studied

Table 1 – Characteristics of the groups studied.[a]

Variables	Groups			p
	Mild intermittent asthma	Mild persistent asthma	Control	
	(n = 20)	(n = 13)	(n = 36)	
Age, years	12.75 ± 0.85	12.69 ± 0.85	12.94 ± 0.86	0.8440
Body mass, kg	50.56 ± 14.00	49.57 ± 12.38	49.64 ± 8.12	0.9483
Height, cm	157.71 ± 7.48	156.91 ± 10.28	158.13 ± 8.03	0.9021
Percentage of body fat	20.17 ± 8.56	22.58 ± 7.27	18.46 ± 6.84	0.2277
IPAQ score	4.00 ± 0.87	4.00 ± 0.75	4.00 ± 0.83	0.2993

IPAQ: International Physical Activity Questionnaire. [a]Values expressed as mean ± SD.

Table 2 – Pulmonary function variables in the groups studied.[a]

Variables	Groups			P
	Mild intermittent asthma	Mild persistent asthma	Control	
	(n = 20)	(n = 13)	(n = 36)	
Pre-BD FVC, L/min	3.19 ± 0.62	3.14 ± 0.48	3.24 ± 0.58	0.8634
Pre-BD FVC, % of predicted	100.00 ± 11.54	102.23 ± 7.15	102.17 ± 10.37	0.7246
Post-BD FVC, L/min	3.15 ± 0.63	3.15 ± 0.51	3.20 ± 0.58	0.9423
Post-BD FVC, % of predicted	98.95 ± 11.79	102.00 ± 7.38	100.39 ± 10.90	0.7210
Pre-BD FEV_1, L/min	2.65 ± 0.44	2.57 ± 0.41	2.82 ± 0.52	0.1958
Pre-BD FEV_1, % of predicted	95.15 ± 6.94	95.00 ± 10.26	101.39 ± 12.23	0.0546
Post-BD FEV_1, L/min	2.71 ± 0.45	2.74 ± 0.48	2.84 ± 0.54	0.6062
Post-BD FEV_1, % of predicted	97.55 ± 8.58	100.92 ± 10.15	102.11 ± 12.31	0.3325
Pre-BD FEV_1/FVC, %	83.85 ± 7.40	81.85 ± 7.74	86.78 ± 5.36	0.0465
Post-BD FEV_1/FVC, %	86.65 ± 6.14	88.61 ± 7.97	88.94 ± 5.36	0.3985
Pre-BD PEF, L/min	5.38 ± 0.96	5.37 ± 0.93	5.50 ± 0.86	0.8626
Pre-BD PEF, % of predicted	88.15 ± 9.30	91.23 ± 14.13	89.47 ± 10.52	0.7326
Post-BD PEF, L/min	5.29 ± 0.84	5.63 ± 1.33	5.45 ± 1.04	0.6496
Post-BD PEF, % of predicted	86.90 ± 11.27	95.08 ± 18.50	88.61 ± 13.69	0.2472
Pre-BD MVV, L/min	85.20 ± 21.04	84.77 ± 19.89	91.83 ± 16.74	0.3238
Pre-BD MVV, % of predicted	84.35 ± 18.09	84.15 ± 14.02	90.14 ± 13.84	0.2849

Pre-BD: pre-bronchodilator; Post-BD: post-bronchodilator; and MVV: maximal voluntary ventilation. [a]Values expressed as mean ± SD.

had airflow obstruction at the time of the evaluation (exclusion criterion), all had normal pre- and post-bronchodilator spirometry, and the possibility of exercise-induced asthma, a potential confounding variable during a maximal cardiopulmonary exercise test, was controlled by administering albuterol (400 µg) 20 min before the test. In the present study, the difference, albeit small, between the asthma patients and the controls regarding at-rest spirometry results was suggestive of reduced aerobic capacity during exercise. However, this proved not to be the case.

Defined as the maximum volume of air that an individual can inhale and exhale in 1 min during maximal voluntary effort, MVV provides a nonspecific overview of respiratory function. Moderate and severe obstructive pulmonary disease can result in abnormal MVV values; this is due to excessive air trapping and respiratory muscle disadvantage, which is common in patients with such breathing patterns.[18] The MVV that individuals can achieve depends on the integrity of their respiratory physiology. In all three groups, MVV values remained within the reference range, indicating that the individuals with asthma and those without had similar ventilatory capacity.

We found that MVV was higher than the maximal levels of ventilation during exercise,

Table 3 – Cardiorespiratory variables analyzed during maximal exercise testing in the groups studied.[a]

Variables	Groups			p
	Mild intermittent asthma	Mild persistent asthma	Control	
	(n = 20)	(n = 13)	(n = 36)	
$V_E$max, L/min	79.08 ± 16.65	74.07 ± 14.49	77.52 ± 17.14	0.6943
VR, %	97.65 ± 24.69	82.69 ± 29.21	85.72 ± 19.47	0.1137
V_E/VO_2	39.30 ± 4.96	39.69 ± 3.99	37.58 ± 4.33	0.2215
RQ	0.98 ± 0.05	0.99 ± 0.03	0.97 ± 0.41	0.2035
Maximal HR, bpm	203.75 ± 7.77	201.69 ± 9.56	203.61 ± 10.44	0.6947
VO_2max, $mL \cdot kg^{-1} \cdot min^{-1}$	41.43 ± 6.80	42.25 ± 7.58	42.06 ± 7.25	0.7374
Serum lactate, mmol/L	7.23 ± 1.74	8.03 ± 2.69	7.94 ± 2.28	0.3332
Speed, km/h	10.89 ± 1.37	10.52 ± 1.44	11.55 ± 1.63	0.0535
Exercise duration, min	19.10 ± 4.09	18.15 ± 3.85	20.47 ± 4.35	0.0758

$V_E$max: maximal minute ventilation; VR: ventilatory reserve; V_E/VO2: ventilatory equivalent for oxygen; RQ: respiratory quotient; and VO_2max: maximal oxygen uptake. [a]Values expressed as mean ± SD.

a finding that is consistent with the literature. This is due to the fact that, during exercise, the respiratory system is not required to work to the utmost. Studies suggest that specific exercises for individuals with obstructive pulmonary disease are interesting because training can increase respiratory muscle strength, respiratory muscle endurance, and MVV.[19]

If any type of organ dysfunction or adaptation is expected to occur as a result of the severity of asthma, it will necessarily be expressed by VO_2max, which is a measure that includes the performance of the various systems involved in the mechanism of oxygen consumption. It reflects cardiovascular, pulmonary, and muscular components, being considered the best single index of health-related physical fitness.[20] The VO_2max values obtained in the present study were similar to those reported in several studies involving children and adolescents.[20-22]

In the present study, VO_2max was found to be similar among the three groups, a finding that is consistent with those of a study evaluating exercise performance in 80 children with mild to moderate asthma and 80 healthy children. The two groups were found to be similar in terms of aerobic capacity, as assessed by maximal exercise testing (40.5 ± 8.4 $mL \cdot kg^{-1} \cdot min^{-1}$ vs. 42.6 ± 9.6 $mL \cdot kg^{-1} \cdot min^{-1}$).[23] Garfinkel et al.[2] reported similar findings, i.e., no significant differences between stable patients with mild to moderate asthma and controls in terms of VO_2max (36.85 ± 10.80 $mL \cdot kg^{-1} \cdot min^{-1}$ vs. 38.48 ± 5.34 $mL \cdot kg^{-1} \cdot min^{-1}$; $p = 0.32$). Baraldi reported that VO_2 and V_E during submaximal and maximal exercise testing were similar between children with asthma and those without, the two groups of children being therefore similar in terms of aerobic capacity.[24]

The results of the present study are inconsistent with those of a study involving 8 children with asthma and 7 children without; VO_2max was significantly lower in the former than in the latter (44 ± 5.4 $mL \cdot kg^{-1} \cdot min^{-1}$ vs. 55.6 ± 10.3 $mL \cdot kg^{-1} \cdot min^{-1}$), a finding that was negatively correlated with bronchial obstruction.[25] In another study,[26] a significant difference was found between boys with asthma and those without in terms of VO_2max (31.6 ± 5.1 $mL \cdot kg^{-1} \cdot min^{-1}$ vs. 35.2 ± 6.1 $mL \cdot kg^{-1} \cdot min^{-1}$) but not between girls with asthma and those without (25.3 ± 2.8 $mL \cdot kg^{-1} \cdot min^{-1}$ vs. 23.9 ± 4.9 $mL \cdot kg^{-1} \cdot min^{-1}$). The variation in aerobic capacity across studies comparing individuals with asthma and those without can be explained, in part, by the differences in methods, types, intensities, duration of exercise, level of training, and, first and foremost, identification, characterization, and classification of asthma severity.

The mean VO_2max values in the groups under study allow us to conclude that the severity of asthma had no impact on aerobic capacity between attacks. For instance, the mean VO_2max in the mild persistent asthma group was nearly equal to that in the control group.

The fact that the three groups studied were similar in terms of VO_2max indicates that the responses of the remaining VO_2 components do not differ from one another or that possible deficiencies are fully compensated. This answers the question regarding respiratory failure, which has been reported in other studies.[24-26] On the basis of exercise tolerance variables such as $V_E$max, $V_E$max/MVV, V_E/VO_2, and VO_2max, we can affirm that neither asthma severity nor ventilatory limitation during exercise influenced aerobic capacity (VO_2max) in any of the three groups studied.

The behavior of $V_E$max in the present study was similar to that reported in other studies, which found no significant differences in $V_E$max between individuals with asthma and those without, as well as no ventilatory limitation to the work capacity of asthma patients.[27] Ventilatory limitation to exercise capacity can occur in cases of severe asthma, in which complex mechanisms are involved in the pathophysiology of the disease, being unlikely to occur in cases of controlled, mild to moderate asthma.[28] The $V_E$max values found in the present study confirm the findings of Lewis et al.[28]

Ventilatory reserve is the difference between the maximum ventilation rate that an individual can theoretically achieve (MVV) and the ventilation rate that is actually achieved at a given time point. The $V_E$max/MVV ratio has been used as an index of ventilatory reserve, or rather of its inverse, meaning that high $V_E$max/MVV values indicate low ventilatory reserve. Although $V_E$max/MVV varies widely in males and females, values above 85% for males and above 75% for females (i.e., a ventilatory reserve of 15% and a ventilatory reserve of 25%, respectively) are uncommon in healthy sedentary individuals.[29] Some studies have reported findings that are similar to ours, i.e., no significant differences in ventilatory reserve between children with mild to moderate asthma and those without.[27]

In order to assess breathing economy during exercise, we calculated V_E/VO_2, which is the ratio between the volume of air ventilated and the amount of oxygen consumed. A higher V_E/VO_2 translates to lower breathing economy. In the present study, V_E/VO_2max values ranged from 37 to 69, indicating breathing economy and being consistent with those reported in a study involving children and youths.[30]

Finally, judging from the final result obtained, the period between attacks was clinically well characterized and well selected in the present study. This allowed group homogeneity, which is required to compare individuals with asthma of varying severity and those without in terms of their aerobic capacity. As a result, there were no statistically significant differences between the patients with mild intermittent asthma and those with mild persistent asthma or between the asthma patients and the controls in terms of the spirometric values. This demonstrates that the classification of asthma severity is not supported by the functional variables investigated during the period between attacks. Therefore, the limitations imposed by the criteria for determining asthma severity[3] in the period between attacks do not allow functional differentiation between patients with mild intermittent asthma and those with mild persistent asthma. It could be argued that there are no differences, given that both groups of patients are clinically equal. However, this is not supported by the literature; the results of studies on this topic refer to study groups rather than populations and are discrepant.[5]

The limitations of the present study lie in the fact that our sample was a study group. Therefore, the results reflect the characteristics of the group and those of the methods employed. Because this was not a population-based study, the results obtained cannot be generalized. We conclude that a diagnosis of bronchial asthma (mild intermittent or mild persistent) has no effect on the aerobic capacity of children and adolescents between asthma attacks.

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