

EFFECT OF PHYSICAL TRAINING ON EXERCISE-INDUCED BRONCHOSPASM IN YOUNG ASTHMATICS




EFEITO DO TREINAMENTO FÍSICO NO BRONCOESPASMO INDUZIDO PELO EXERCÍCIO EM JOVENS ASMÁTICOS

EFFECTO DEL ENTRENAMIENTO FÍSICO EN EL BRONCOESPASMO INDUCIDO POR EL EJERCICIO EN JÓVENES ASMÁTICOS

SYSTEMATIC REVIEW ARTICLE
ARTIGO DE REVISÃO SISTEMÁTICA
ARTÍCULO DE REVISIÓN SISTEMÁTICA

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ABSTRACT

Introduction: Asthma is the most common chronic disease in childhood and its prevalence has increased in recent years. Although regular physical activity (PA) is considered to be beneficial for the health of asthmatics, especially children and adolescents, it can also be one of the elements that triggers asthma. This is known as exercise-induced bronchospasm (EIB), and is considered one of the factors that limits asthmatics' participation in PA. **Objective:** This study aims to review the effects of physical conditioning on EIB in asthmatic children and adolescents. **Methods:** A systematic review was carried out on the Pubmed, Bireme and Web of Science databases, considering publications from 1998 to April 2019. **Results:** Eight articles were retrieved; five of the articles presented no significant difference in EIB parameters after physical training, and three demonstrated significant benefits in EIB. **Conclusion:** There is insufficient evidence that physical training helps reduce the frequency and severity of EIB in young asthmatics. There are still few studies that seek to show the effect of a physical training program on the improvement of EIB in children and adolescents. It is suggested that further randomized clinical trials be conducted, to investigate the effects of physical training on EIB parameters in children and adolescents. **Level of Evidence II; Systematic review.**

Keywords: Asthma; Adolescents; Young people; Physical exercise; Bronchospasm.

RESUMO

Introdução: A asma brônquica é a doença crônica mais comum na infância e a sua prevalência tem aumentado nos últimos anos. Apesar da prática regular de atividade física (AF) ser considerada benéfica para a saúde do asmático, especialmente, em crianças e adolescentes, ela também pode ser um dos elementos desencadeantes da asma, conhecido como broncoespasmo induzido pelo exercício (BIE) que é considerado como um dos fatores que limita a participação de asmáticos na AF. **Objetivo:** A presente pesquisa tem como objetivo revisar os efeitos do condicionamento físico sobre o BIE em crianças e adolescentes asmáticos. **Métodos:** Realizou-se uma pesquisa bibliográfica nas bases Pubmed, Bireme e Web of Science, considerando publicações no período de 1998 a abril de 2019. **Resultados:** Foram selecionados oito artigos, sendo que cinco não apresentaram diferença significativa nas variáveis do BIE após o treinamento físico e três demonstraram benefícios significativos. **Conclusão:** Não há evidências suficientes de que o treinamento físico contribua para redução na frequência e/ou gravidade do BIE em jovens asmáticos. Ainda são poucos os estudos que buscam mostrar o efeito de um programa de treinamento físico na melhora do BIE em crianças e adolescentes. Sugere-se a realização de mais ensaios clínicos randomizados que investiguem os efeitos do treinamento físico sobre as variáveis do BIE em crianças e adolescentes. **Nível de evidência II; Revisão sistemática.**

Descritores: Asma; Jovens; Treinamento físico; Broncoespasmo.

RESUMEN

Introducción: El asma bronquial es la enfermedad crónica más común en la infancia y su prevalencia ha aumentado en los últimos años. A pesar de que la práctica regular de actividad física (AF) sea considerada benéfica para la salud del asmático, especialmente en niños y adolescentes, también puede ser uno de los elementos desencadenantes del asma, conocido como broncoespasmo inducido por el ejercicio (EIB), que es considerado como uno de los factores que limitan la participación de asmáticos en la AF. **Objetivo:** La presente investigación tiene como objetivo revisar los efectos del acondicionamiento físico sobre el EIB en niños y adolescentes asmáticos. **Métodos:** Se realizó una búsqueda bibliográfica en las bases de datos Pubmed, Bireme y Web of Science, considerando publicaciones en el período de 1998 a abril de 2019. **Resultados:** Fueron seleccionados ocho artículos, siendo que cinco no presentaron diferencia significativa en las variables del EIB después del entrenamiento físico y tres demostraron beneficios significativos. **Conclusión:** No hay evidencias suficientes de que el entrenamiento físico contribuya para la reducción en la frecuencia y/o gravedad del EIB en jóvenes asmáticos. Todavía son pocos los estudios que buscan mostrar el efecto de un programa de entrenamiento físico en la mejora del EIB en niños y adolescentes. Se sugiere la realización de más ensayos clínicos aleatorios que investiguen los efectos del entrenamiento físico sobre las variables del EIB en niños y adolescentes. **Nivel de evidencia II; Revisión sistemática.**

Descriptores: Asma; Jóvenes; Entrenamiento físico; Broncoespasmo.



INTRODUCTION

Bronchial asthma is the most common chronic disease in childhood and adolescence, and its prevalence has increased in recent years.^{1,2} This disease is characterized as an airway inflammatory disease that causes airflow limitation and bronchial hyperresponsiveness, leading to wheezing, dry cough and shortness of breath, and which has impact on sleep quality, daily activities and quality of life³.

Although physical activity (PA) is an indispensable component for the health and integral development of children and adolescents,⁴ this activity can trigger a bronchospasm crisis, which is known as exercise-induced bronchospasm (EIB).^{5,6} This condition is highly common in asthmatics (40 to 90%), but can also occur in 5 to 20% of the general population.⁷ The world prevalence of EIB in children and adolescents is 9%, being 8% in countries of Europe, and 12% in America and Asia.⁸

EIB is defined as a condition that causes transient lower airway obstruction soon after moderate to vigorous physical activity, with the presence or absence of asthma.^{9,10} EIB is characterized by shortness of breath, cough and wheezing soon after physical activity, and is clinically confirmed by a $\geq 10\%$ drop in Forced Expiratory Volume in the First Second (FEV1).¹¹ The exact mechanism responsible for EIB is still uncertain, but factors such as airway cooling and dryness during physical activity seem to trigger bronchospasm.¹⁰

Although exercise is a triggering agent of bronchospasm, regular physical activity is considered an important component in the treatment of asthma.¹² The systematic reviews and meta-analyses conducted so far have reported that physical training in young asthmatics was able to increase cardiorespiratory fitness^{13,14} and reduce exercise dyspnea,^{15,16} as well as improve quality of life.^{16,17} However, physical training does not seem to affect lung function during rest,¹³⁻¹⁵ and the results on EIB are still inconsistent.^{16,17}

Since asthma is a prevalent disease in the pediatric population, and EIB has been a limiting factor for participation in physical activity and sports,^{18,19} the understanding of the effects of physical training on EIB may contribute to the establishment of guidelines for the assessment and prescription of physical exercise for asthmatic children and adolescents with EIB. Therefore, the aim of this study was to perform a systematic review of the effects of physical training on EIB in asthmatic children and adolescents.

METHODS

Search Strategies

For the development of this research, a bibliographical search was performed in PubMed, BIREME and Web of Science. The searches for the articles were performed by two independent researchers (WAL and FEP) until April 2019. The selection of the descriptors was based on the DeCS (the Health Science Descriptors by BIREME) and were the terms in English and Portuguese, combined according to Boolean operators: (adolescents OR children) AND (exercise-induced asthma OR exercise-induced bronchospasm OR exercise-induced bronchoconstriction OR exercise-induced bronchial hyperreactivity OR exercise-induced airway hyperactivity OR exercise-induced airway hyper-responsiveness OR exercise-induced bronchial hyper-responsiveness) AND (exercise training OR physical training OR resistance training OR aerobic training OR concurrent training OR combined training OR interval training), with no fields restriction (*all fields*). We considered publications from 1998 to April 2019 that evaluated EIB before and after fitness programs and performed direct evaluation of EIB in children and adolescents. The articles were read in full or in abstract form and a file was prepared to extract information from the selected articles.

Methodological Quality

The studies included in this review were assessed using the PEDro (Physiotherapy Evidence Database) scale, based on the Delphi list. The PEDro scale consists of 10 items, each item contributing 1 point (except for item 1 which is not scored). The total score ranges from 0 (zero) to 10 (ten). This scale assesses the methodological quality of randomized controlled trials, observing two aspects: whether they have internal validity and if they contain sufficient statistical information to make it interpretable. The scale does not assess external validity, significance, or size of treatment effects.

The studies were independently qualified by two evaluators who were already familiarized with the scale. Disagreements regarding the PEDro classification were discussed by the evaluators, and the studies scores were defined by consensus (Table 1). The cutoff point established to separate high and low quality studies was <6 (low quality) or ≥ 6 (high methodological quality), according to Vasconcellos et al.²⁰

Table 1. PEDro scale to assess the methodological quality of the included studies.

Year	Author	1	2	3	4	5	6	7	8	9	10	Total
1999	Matsumoto et al. ²¹	+	+	+	+	-	+	+	-	+	+	8
1999	Neder et al. ²²	+	-	-	-	-	+	+	-	+	+	5
2000	Hallstrand et al. ²³	+	-	-	-	-	+	+	-	-	+	4
2002	Natali et al. ²⁴	+	-	+	-	-	+	+	-	+	+	5
2006	Silva et al. ²⁵	+	-	-	-	-	+	+	+	-	+	5
2007	Sidiropoulou et al. ²⁶	+	-	-	-	-	+	+	-	+	+	5
2007	Fanelli et al. ²⁷	+	+	-	-	-	+	-	+	+	+	6
2014	Tahan et al. ²⁸	-	-	-	-	-	+	+	+	+	+	5

1 Control group 2 Randomization 3 Groups similarity before intervention 4 Sample size calculation performed 5 One year follow up 6 Exercise exclusivity 7 Structured and supervised program 8 Intervention of at least 12 weeks 9 Reliable assessment instruments 10 Appropriate statistical analysis.

RESULTS

From the 2,784 titles identified, 2,420 were excluded because they were duplicated. Three hundred and sixty-four articles were excluded for being review or observational articles, having used other therapies besides physical training, or having indirectly evaluated EIB. From the total, eight articles were included in the analysis and read in full (Figure 1). The articles analyzed met the inclusion criteria: experimental method, performed with children and adolescents with asthma, performed pre and post EIB test, intervention only with physical training and without association with medication to induce EIB.

The data from the studies analyzed in this review are presented on Table 2, which includes aspects such as: methodological procedure, characteristics and main results. Differences observed between the articles were due to: age, physical exercise parameters, evaluation methods and EIB classification criteria. From the eight studies,²¹⁻²⁸ only one did not present a control group.²⁸ Regarding the intervention, the articles varied greatly in terms of duration, weekly frequency, duration of exercise session, type and intensity of training. The duration of the interventions ranged from 6 to 16 weeks, with variations in weekly frequency (from two to six days) and the duration of the training session (from 30 to 90 minutes). In relation to the training developed during the intervention, most studies included the following types of exercise: aerobic,²¹⁻²⁴ combined aerobic and resistance²⁵⁻²⁷ or only resistance exercise.²⁸ The intensity was reported in six studies,^{21-24,26,27} ranging from 50% to 90% of HR_{max} ,^{22,24} above the lactate threshold (LT)^{21,26,27} and 70% of VO_{2max} .²³ Seven studies were conducted with children and adolescents with moderate to severe asthma^{21,23-28} and only one with young athletes with positive EIB.²²

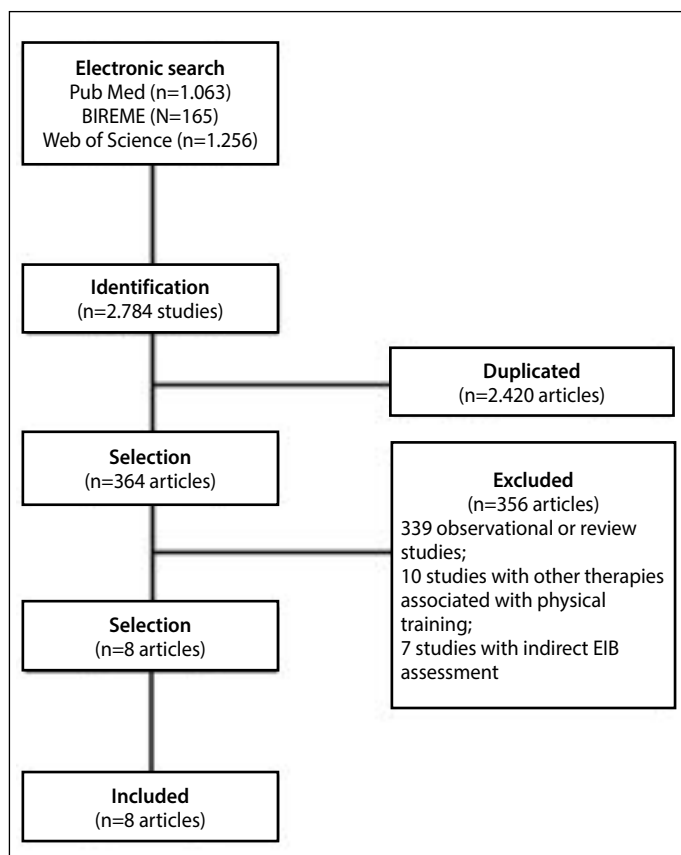


Figure 1. Flowchart of included articles in each stage of the study.

Table 2. General characteristics of the studies included in the review.

Author/Year	Sample	Exercised-induced asthma assessment instruments	Intervention	Results
Matsumoto et al. ²¹	n=16 (total) Age= 8-10 years n=8 (experimental) n=8 (control) Randomized	6 weeks; bronchial provocation test with 6-minute exercise on cycle ergometer; above LT; FEV ₁ assessment right after, 5 and 15 minutes after exercise.	Type= swimming (crawl) Intensity= acima do LT Duration= 30 minutes Frequency= 6x/week	↑ work load ↔ % FEV ₁ after exercise
Neder et al. ²²	n= 42 (total) Age = 8-16 years n=26 (experimental) n=16 (control)	8 weeks; bronchial provocation test with 6-minute exercise on cycle ergometer; 80% HR _{max} ; FEV ₁ assessment 5, 10 and 20 minutes after exercise; positive EIB for FEV ₁ >10% fall.	Type = running, with or without ball Intensity= 50-60% and 80-90%HR _{max} Duration = 45 minutes Frequency = 3x/week	↑ Aerobic fitness ↓ Anti-inflammatory medication ↔ % FEV ₁ after exercise ↔ EIB Frequency
Hallstrand et al. ²³	n= 10 (total) Age = 10-16 years n=5(experimental) n=5 (control)	10 weeks; bronchial provocation test with 12-minute exercise on cycle ergometer; progressive intensity until exhaustion; FEV ₁ assessment 3, 6, 10 and 15 minutes after exercise; positive EIB for FEV ₁ >10% fall.	Type = aerobic exercise Intensity= 70-80%VO _{2max} Duration = 30 minutes Frequency = 3x/week.	↑ Aerobic fitness ↓ Exercise dyspnea ↔% FEV ₁ after exercise
Natali et al. ²⁴	n= 32 (total) Age = 10-16 years n=16(experimental) n=16 (control)	10 weeks; bronchial provocation test with 8-minute exercise on treadmill, 85 to 90% HR _{max} ; PEF assessment 5 and 10 minutes after exercise; positive EIB for FEV ₁ >10% fall.	Type = swimming (crawl) Intensity= 80-85% HR _{max} Duration = 45 minutes Frequency = 3 x/week	↓ PEF after exercise
Silva et al. ²⁵	n= 69 (total) Age = 8-11 years n=46 (experimental, bring 23 morning training and 23 afternoon training) n=23 (control)	16 weeks; Bronchial provocation test with 6-minute exercise on treadmill, 80% HR _{max} ; FEV ₁ assessment 5, 10, 15, 20, 30 and 45 minutes after exercise; positive EIB for FEV ₁ >10% fall.	Type = walking/running, swimming, stretching and calisthenics Intensity = not mentioned Duration = 90 minutes Frequency = 2 x/week	↑ Distance covered ↑ Abdominal muscle endurance ↔ % FEV ₁ after exercise
Sidiropoulou et al. ²⁶	n= 29 (total) Age = 10-12 years n=18 (experimental) n=11 (control)	8 weeks; Bronchial provocation test with 6-minute running, 80-90% HR _{max} ; FEV ₁ assessment 2, 5, 10, 15 and 20 minutes after exercise; positive EIB for FEV ₁ >10% fall.	Type = cycling, calisthenics and stretching Intensity = above LT Duration = 45 minutes Frequency = 3 x/week	↑ Distance covered ↓ % FEV ₁ after exercise
Fanelli et al. ²⁷	n=38 (total) Age = 8-15 years n=17 (experimental) n=21 (control) Randomized	16 weeks; Bronchial provocation test with 6-minute exercise, 80% HR _{max} ; FEV ₁ assessment 2, 5, 10 and 20 minutes after exercise; positive EIB for FEV ₁ >10% fall.	Type = running and cycling, stretching and resistance exercise Intensity= between LT and RCP and 15RM Duration = 90 minutes Frequency = 2x/week	↑ Aerobic fitness ↓ Exercise dyspnea ↑ Quality of Life ↔ Anti-inflammatory medication ↔ % FEV ₁ after exercise
Tahan et al. ²⁸	n= 20 (total) Age = 6-17 years n=10 asthmatic children (EIB+) 10 (EIB-) No control group	12 weeks; Bronchial provocation test with 6-minute exercise on treadmill with submaximal load, FEV ₁ assessment 5, 10, 15 and 20 minutes after exercise; FEF _{25%} -75% _{or} FVC, PEF%, PEFR and IgE levels, number of número de eosinophils. positive EIB for FEV ₁ >15% fall.	Type = hatha yoga Intensity= not mentioned Duration = 60 minutes Frequency = 2 x/week	↓ % FEV ₁ after exercise (Only EIB+ group)

The protocol of the exercise provocation tests varied among the studies, being five performed on treadmill,²⁴⁻²⁸ and three on cycle ergometer.²¹⁻²³ The duration of the test ranged from 6 to 12 minutes, all with submaximal intensity above 80% of HR_{max} or above LT. Post-exercise FEV₁ assessment was always performed soon after the end of the test, beginning from three to five minutes after the test, most of them five minutes after the test. Only two studies started the assessment at the second and third minute after the bronchial provocation test^{23,26} and the follow-up of pulmonary function after the test ranged from 10 to 45 minutes. (Tabela 2)

From the investigated studies, five did not show significant changes in EIB variables after physical training^{21-23,25,27} whereas only three studies presented a statistically significant reduction in the pulmonary variables associated with EIB after intervention.^{24,26,28} However, the methodological quality of most of the reviewed studies was considered low (<six points on the PEDro scale), with only two studies^{21,27} considered to be of good quality (Table 1), but which did not present significant changes in EIB after physical training intervention.

DISCUSSION

The purpose of this systematic review was to investigate the effect of physical training on EIB of asthmatic children and adolescents. Although other systematic reviews and meta-analyses have verified the effects of physical training on young asthmatics,¹³⁻¹⁷ most of them emphasized pulmonary variables during rest and other factors, such as physical fitness and quality of life. From the eight studies analyzed in this review, only three studies showed significant improvement of pulmonary variables associated with EIB after physical training.

Asthma is a disease with high prevalence in childhood and adolescence, and regular physical activity has been recommended as an integral part of a healthy lifestyle.^{1,4} Regular physical activity reduces the frequency of asthma attack,⁵ besides bringing numerous benefits to health and quality of life.¹⁶ In addition, PA has the role of improving physical fitness in childhood, which is essential for the maintenance of physical fitness in adulthood, as well as improving psychological, social and therapeutic aspects, and reducing wheezing, hospitalization, and even the use of medication for asthma.¹²

Despite the benefits of physical training for asthmatics,¹³⁻¹⁴ physical exercise has the potential to induce bronchospasm.¹⁸⁻¹⁹ Studies conducted in different populations, with children, adolescents and adults, have shown that some effects of physical training can be proven in asthmatics, such as improving cardiorespiratory fitness and tolerance to the effort, as well as reducing exercise dyspnea, aerobic fitness and quality of life.¹³⁻¹⁷ However, the effects of physical training on EIB are still inconsistent.^{16,17}

In a systematic review and meta-analysis by Eichenberger et al.,¹⁶ the effect of physical training on airway hyperreactivity in individuals with asthma, it was found that after physical training, significant changes occurred in quality of life (17% of the articles) and in bronchial hyperresponsiveness (53% of the articles). Nonetheless, there were only few articles (9%) which presented significant results of changes after physical training in the EIB variables. In the present review, only three studies found a reduction in the values of FEV₁^{28,26} and peak expiratory flow (PEF)²⁴ after physical training intervention in asthmatic children and adolescents.

What has been speculated is that the improvement of aerobic fitness allows asthmatic individuals to better tolerate asthma attacks, as well as submaximal exercise, which lowers the chances of EIB triggering.⁵ However, it occurs without any changes in the pulmonary variables which characterize the presence of EIB, such as the reduction in FEV₁ or PEF.¹⁹ Another possible effect could be the anti-inflammatory role of exercise in the reduction of the pulmonary inflammation present in asthmatic individuals.²⁹ In fact, recent studies have shown significant improvement of systemic chronic inflammation³⁰ and airway inflammation^{31,32} in adults with moderate to severe asthma. Notwithstanding, the relationship between chronic inflammation and air hyperreactivity has not yet been well established.³⁰ Additionally, none of the studies included in this review evaluated the systemic or pulmonary inflammatory status of children and adolescents undergoing a physical training program.

Although swimming is one of the most recommended exercise modalities for asthmatic individuals, the benefits of swimming for this population seem to be more associated with the environment in which this modality is performed than with the modality itself.⁵⁻⁶ In the present review, two studies used swimming as a modality for asthmatic children and adolescents, and the results were contradictory. Matsumoto et al.²¹ found a small reduction in FEV₁ after exercise, yet with no significant statistical difference when compared to the control group. On the other hand, Natali et al.²⁴ found increased PEF after exercise. Differences in the population studied (children versus adolescents), as well as the differences in weekly frequency and duration of interventions, make it difficult to compare these studies. These findings corroborate a meta-analysis by Beggs et al.³³ on the effects of swimming training on asthmatic children and adolescents, which fails to show the superiority of swimming over other exercise modalities in young asthmatics, and also suggests that swimming was able to improve physical fitness and pulmonary function during rest, but with little effect on asthma symptoms and attacks.

Walking and running are two types of physical exercise considered more asthmogenic than others, such as swimming and cycling.⁵ Although the mechanisms for this are unclear, it is believed that the intensity

achieved through these modalities, especially because they carry body weight, induce greater ventilation and, consequently, greater susceptibility to the triggering of bronchospasm.⁷ In addition, the environments in which these activities are normally performed have a number of potential allergens that could induce an asthma attacks during or shortly after exercise.¹⁹ Most of the reviewed studies used walking and/or running alone, or associated with other activities, such as swimming, or resistance exercise. However, none of these studies found significant changes in the variables associated with EIB in young asthmatics.

The combination of aerobic training and resistance exercises has been advocated in the American College of Sports Medicine Position Stand,³⁴ as an important strategy for maintaining and/or improving health parameters. Combined training can contribute to both cardiorespiratory fitness improvement and strength/muscular endurance similarly to isolated forms of training. Besides, combined training has been effective in chronic inflammation associated with obesity³⁵ and aging.³⁶ In the present review, from the three studies that combined aerobic and resistance exercise, only one of them found significant improvement in pulmonary function after physical training.

Only one study investigated the effects of yoga on EIB in asthmatic children and adolescents. Although this modality is often used in asthmatic patients, the effectiveness of this practice in their health is uncertain. Cramer et al.³⁷ performed a meta-analysis and found that the practice of yoga contributed to the improvement of asthma symptoms, pulmonary function during rest and quality of life of asthmatic patients. Nonetheless, there was no difference between yoga and other techniques used in respiratory training. The practice of yoga seems to be an effective alternative on EIB variables, according to the present review. However, further studies are needed in order to test this modality alone, or to compare it with other physical training modalities used in asthmatic children and adolescents.

Regarding the intensity, duration and weekly frequency of physical training, there was heterogeneity in these components in the reviewed studies, making it difficult to compare them. However, positive training outcomes were found in studies using moderate to high intensity, lasting 45 minutes per session, performed three times a week for at least eight weeks. These parameters are in accordance with the ACMS guidelines for the general population,³⁴ which recommends 150 minutes of moderate intensity exercise or 75 minutes of vigorous intensity exercise, or the combination of both per week. However, it was not possible to establish an exercise dose-response on EIB-related responses in young asthmatics.

Physical exercise prescription for asthmatics depends on asthma control and positive or negative diagnosis of EIB.⁵ Individuals with controlled asthma and no history of EIB can perform physical activity without restriction.¹² However, asthmatics with EIB should prioritize moderate-intensity exercise, between 40 to 59% of VO_{2max} or 55 to 69% of HR_{max}, so to avoid the triggering of EIB.¹⁸ Besides that, the use of bronchodilators is recommended for asthmatic individuals with a history of EIB who intend to exercise at higher intensities.⁵ Therefore, information on the type of exercise used during physical training and the intensity of the sessions are important factors that need to be informed and controlled during the intervention. Future studies that investigate the effects of different types of exercises, intensities, duration and weekly frequency on EIB variables are needed.

The importance of physical activity for asthmatics is undeniable. The prescription of physical activity for this population should take into account the presence of asthma and EIB. Even though exercise does not improve pulmonary function during rest, some of its benefits justify its recommendation, such as increased physical activity levels, reduced sedentary behavior, improvement in physical fitness and quality of life. Nevertheless, there are still several gaps in aspects related to EIB, as well as the effects of physical training on functional, immunological and inflammatory

variables associated with this condition,³⁸ since the prevalence of EIB is high in asthmatics, but also affects athletes and the general population.⁸

CONCLUSION

Given the above, there is no sufficient evidence that physical training contributes to the reduction of pulmonary variables associated with EIB

in asthmatic children and adolescents. Further randomized clinical trials are suggested to investigate the effects of physical training on EIB in asthmatic children and adolescents.

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