Exercise-induced asthma: current aspects and recommendations*

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ABSTRACT

Objective: To describe the mechanisms of Exercise-Induced Asthma (EIA) as well as the effect of different kinds of physical training on pulmonary function, anaerobic fitness, and aerobic fitness. We highlighted the importance of a correct diagnostic through exercise testing and, concerning treatment, the utilization of drugs such as beta-adrenergics and anticholinergics. **Data source:** The articles were chosen using the PubMed and Scielo databases, considering the year of publication and giving preference to clinical randomized trials with well-defined inclusion criteria. **Summary of the findings:** The medication used and the frequent symptoms during and after exercise appear as a limiting factor to the practice of exercises among subjects with EIA. This may result in a sedentary lifestyle. **Conclusion:** Subjects with EIA should be allowed to do exercise if well prescribed.

Keywords: Asthma. Exercise. Prevention.

INTRODUCTION

Exercise-induced asthma (EIA) is known as a transitory airways obstruction immediately after vigorous exercise, being one of its main symptoms lack of air; cough and wheeze. It ca be evidenced by the decrease in the expiration volume forced in 1 second (VEF_1) and by other spirometric parameters[1]. The mechanism of development of this obstruction has not been defined yet; however, several studies[1-5] were conducted in order to clarify the mechanisms of action of EIA.

EIA may be observed in children and adolescents of different physical conditioning backgrounds, from those not engaged in sports to competitive athletes. Physical exercise causes bronchoconstriction in the majority (~70%) of the children and adolescents who present asthma; nevertheless, EIA may occur in those who do not present asthma diagnosis[6]. Typically, the crisis begins 2 to 4 minutes after the exercise, with peaks from 5 to 10 minutes, and spontaneously disappears in about 20 to 40 minutes. Sometimes the crisis may be sustained for more than an hour. Late responsiveness may appear from 4 to 10 hours post exercise[7].

The prevalence of EIA reaches 12% in school-aged children and varies in different sports modalities, being 50% in cross-country skiing athletes; 35% in ice hockey; 43% in velocity skaters and 17% in winter and summer Olympic athletes[1]. It is interesting to observe that the highest EIA prevalence occurs in those athletes who compete in cold weather.

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There are usually two used descriptions: EIA and bronchoconstriction exercise-induced (EIB) EIB is bronchial obstruction (spasm) observed after exercise in individuals who present normal pulmonary function in resting; and EIA is sometimes used to describe the increase of the post-exercise symptoms for asthmatic subjects. However, the two terminologies are interchangeable. In this review we chose to use only the expression exercise-induced asthma.

The aim of this review is to describe the EIA mechanisms as well as the kinds of diagnosis and management; to discuss the impact of different kinds of training in the pulmonary function and in the cardiorespiratory capacity and finally to bring recommendations for safe practice of physical exercises.

MECHANISMS OF ACTION OF EIA

The physiological events which trigger the EIA crisis remain unknown; nevertheless, several studies[2-3,5,8-14] suggest some physiological mechanisms of EIA.

EIA may be explained by two hypotheses[2-3]. The osmotic hypothesis considers that dehydration of the airways generated by the insensitive water loss by the respiratory tract stimulated by inhaling of dry air during exercise increases the osmolarity of the periciliary liquids. Such process releases hence chemical mediators (histamine, prostaglandins and leukotrienes) which increase the contraction of the bronchial straight musculature, causing obstruction.

The thermal hypothesis considers that EIA is initiated by the thermal effect in the airways caused by exercise, that is, the cooling of the airways followed by a rewarm-up post exercise which causes a reactive hyperemia of the bronchial vasculature and edema on the airways wall[2-3,13]. Such episode suggests that the cooling of the airways[14] would be an important stimulus for EIA. Nonetheless, Zeitoun *et al.*[5] found that EIA occurred when warm and dry air was inhaled, suggesting that the cooling of the airways would not be the single responsible factor for EIA induction.

An inflammatory response can also be an additional mechanism for the EIA triggering. The presence of inflammatory agents such as macrophages, eosinophils and linfocites in the bronchoalveolar liquid of children with EIA has been confirmed, even in those who present normal pulmonary function in resting[9,15]. These response are reinforced by exposition to allergenic (dust, smoke), viral and bacterial agents as well as to exercise.

In an epidemiological study, Burney[8] suggested an association between salt ingestion and asthma, suggesting that asthmatic individuals present a tendency to ingest more salt than non-asthmatic ones. In prospective studies, Gotshall *et al.*[10] and Mickleborough *et al.*[11-12] demonstrated that salt increased consumption may represent a risk factor, since salt increases EIA. The mechanism through which salt increases EIA is not completely clear yet. Possibly, a saturation of the ATPase Na^+/K^+ in the straight musculature of the upper airways occurs, overacting the Ca^{++} ATPase as

regulator of the electrolytes influx-efflux in the straight muscular cell. However, the calcium carried in this ATPase accentuates the contractibility of the straight musculature, causing bronchoconstriction[10-12].

The amount of each of these hypotheses influence in EIA occurrence remains inconclusive. The fact is that they do not act in the triggering of this phenomenon isolated, suggesting thus, that the interaction of these factors is crucial for EIA.

DIAGNOSIS AND MANAGEMENT

The EIA diagnosis is usually initiated from the observation of symptoms such as cough, wheeze, difficulty in breathing and chest pain, after exercise. However, subjects who present these abnormal symptoms may not be able to recognize them as EIA, simply believing they are unfit[1-2]. Yet, some studies[16-17] demonstrated a weak correlation between self-observation of symptoms with the presence of EIA. Cabral *et al.*[18] evaluated the influence of asthma severity over IEA occurrence. 164 children, mean age of 11 years, were evaluated and classified in intermittent asthma; medium-persistent; moderate persistent and severe persistent subgroups according to the *Global Initiative for Asthma Classification (GINA)*[19]. The results demonstrated that the EIA prevalence in children with severe or moderate asthma was significantly higher than in those with intermittent asthma. However, the response to exercise may be absent even in children with severe persistent asthma, suggesting that the exercise response, that is the EIA occurrence, is not consistently related to clinical severity of asthma. Another difficulty found for the EIA diagnosis, especially in children, is the fact that family members do not usually observe them during physical activities practice, either in sports schools or in physical education classes[2].

CHART 1
EIA symptoms

Typical	Atypical
▪ Cough during or after exercise	▪ Stomachache
▪ Sibilant sound	▪ Headache
▪ Chest pain during or after exercise	▪ To feel unfit
▪ Lack of air during exercise	▪ Muscular cramps

For the consolidation of EIA diagnosis, an exercise test followed by spirometry in which bronchoconstriction is induced by an exercise protocol is usually performed. Such test has presented higher effectiveness in EIA diagnosis than bronchoconstriction induced by drugs such as methacholine and histamine[18]. The tests of provocative concentration using such drugs usually aim the diagnosis of bronchial reactivity, which does not necessarily correspond to EIA diagnosis. The test protocol involves a run/cycle at 80 to 90% intensity of the heart rate (HR) maximal reserve during 6 to 8 minutes[18,20]. Yet, for children and adolescents engaged in competitive sports, the exercise test must be similar to the sport gesture the subject practices[2]. The spirometry is measured before and after (usually at every 5 minutes until 20 minutes) the test performance. The VEF_1 spirometric parameter is the most used for the EIA diagnosis. It is justified for the low intra-subjects variability when compared with other parameters such as the expiratory flow peak[18]. Decrease of 15% of the VEF_1 after the exercise test may be considered EIA[21]. However, 10% decrease of the VEF_1 compared with the baseline values may be sufficient for the EIA diagnosis, since the results correspond to the double of the coefficient of the VEF_1 variation measured[18]. In resting, that is, before the exercises performance, the VEF_1 of children and adolescents with EIA usually presents normal values, at around 90% of the predicted values; if the resting VEF_1 presents values below 90%, it may be indication of non-diagnosed moderate chronic asthma[1].

The performance of sessions with short exercises intervals has shown to reduce the severity of response. This phenomenon is known as refractory period[1-2,13,22-24] and has been used as a device to reduce EIA effects. Despite an intra-subject variability, such maneuver has good effectiveness in EIA prevention[2]. It has not been well-defined either how the refractory period reduces the EIA magnitude. Nonetheless, it is possible that the inflammatory mediators suffer depletion during this period and need time for its resynthesis[13,22] hence, reducing the EIA crisis.

The spirometric evaluation is crucial for the treatment strategy of EIA In resting, if the VEF_1 presents values lower than 90%, it is recommended that a daily treatment for persistent chronic asthma begins. When the spirometric values are normal, high intensity pre-exercises warm-ups (80% HR maximal) performance may be sufficient to reduce the magnitude of response to exercise.

The most effective treatment for EIA is the utilization of short-duration beta-adrenergic drugs via inhalation, such as salbutamol and dissodium cromoglycate, for its bronchodilator action[25]. In other words, the bronchodilation that such kind of drug induces before exercise would possibly be responsible for the minimization of EIA effects. Another alternative would be a more potent bronchodilator during exercise and the inhibition of the chemical mediators release, which would reduce the bronchoconstriction following the exercise[20,26]. However, for athletes the therapy may represent risks of positive tests in anti-doping exams, since the beta-adrenergic drugs are listed as prohibited substances by the International Olympic Committee, according to the World Anti-doping Agency (WADA). This group of drugs must be reported as being of therapeutic use, thus allowing values higher than 1000 ng/dL[27].

The long-term use of beta-adrenergic drugs may cause taquifilaxy[1-2] – appearance of progressive reduction of responsiveness after repetitive administration of a drug or physiological active substance – reducing the effectiveness of these drugs over EIA. Therefore, the intermittent administration may cause an efficient and safe action in the EIA management[9].

Another group pf drugs for the treatment of EIA are the anticholinergic agents. Among them, the ipratropium bromide, which besides presenting a potential anticholinergic action and reasonable bronchodilator effect, presents weak incidence of side effects[5]. However, the efficiency of this drug presents great interindividual variability through airways, especially by the need of an accentuated vagal activity[28-30], which justifies its scarce recommendation as EIA treatment.

EIA AND PHYSICAL EXERCISE

The benefits of physical exercise in EIA have been studied in order to measure the effects of the response to different types of training in physical fitness and in the pulmonary function of subjects with EIA. Ram *et al.*[31] conducted a meta-analysis including randomized clinic essays and observed that the maximal oxygen uptake ($\dot{V}O_{2máx}$) increases with physical training, suggesting that the response of individuals with EIA is similar to the one from healthy ones and therefore, an increase in the cardiorespiratory capacity is accessible. Yet, the pulmonary function in resting did not present significant improvement.

In a prospective study, Counil *et al.*[32] evaluated the response of 16 boys (mean age = 13 years) with EIA to anaerobic and aerobic trainings. The authors concluded that both kinds of training may increase the physical capacity of these subjects, besides presenting good tolerance from their part. It seems that when the bronchial obstruction is relieved, the mechanism of muscular fitness is not different from healthy children. Such episode reinforces the recommendation of physical exercises practice for subjects with EIA.

Asthmatic children are usually insufficiently active; therefore their anaerobic performance may be faulty. The studies in this area are

inconsistent. While some show normal anaerobic capacity measured either by the Wingate anaerobic test[33-34] or by the accumulated O_2 deficit method[35], others show low anaerobic performance in patients with asthma either through strength-velocity tests[36] or the Wingate anaerobic test[37]. Such inconsistencies are hard to be explained; however, they may reflect inter-study differences in the asthma severity; the nutritional status; the degree of maturation and the level of physical activity.

Stanford *et al.*[38] observed the influence of the menstrual cycle over the pulmonary function of asthmatic athletes. Seven women with regular menstrual cycles of 28 days performed exercise tests to exhaustion, on the fifth day (follicular phase) and on the 21st day (luteal phase). The tests of pulmonary function were conducted before and after the exercise test. A significant decrease was observed in the spirometric parameters VEF_1 and in the forced expiratory flow of 25 to 75% of the forced vital capacity ($FEF_{25-75\%}$), on the 21st day of the menstrual cycle. Such evidence suggests that asthmatic athletes may need adjustments in their training and competitions calendar according to their menstrual cycle, due to potential negative effects of the luteal phase in performance.

Silva *et al.*[39] evaluated the effects of the circadian cycle on day variations in the training responsiveness in asthmatic children who were divided in three groups: morning training (MT); afternoon training (AT) and a group with no training (NT). The circuit training program was performed two weekly times and consisted of a 90-minute session in which the children performed the following activities: 5-minute walk, followed by 10-15 minute run (progressive increase during the program); upper and lower limbs activities (to jump rope; exercises of raising their own bodies; to go up and down a stool); abdominal exercises, bar training; individual and team games; postural exercises and back to normal. Pre and post-intervention evaluations involved 9-minute run test, resting heart rate and abdominal strength. Both groups presented significant improvement when compared with the NT group; however, there was no difference in the training responsiveness when it was performed in the morning or afternoon.

According to the *American College of Sports Medicine* (ACSM)[40], the standard-principles for exercise prescription – type; frequency; intensity and duration – may be applied in patients with respiratory diseases, including EIA.

CHART 2
Recommendations for safe practice of physical exercise

- To choose the appropriate kind and duration of exercise
- To perform pre-exercise warm-ups (refractory period)
- To reduce the most the heat and water loss by respiratory via
- To use therapy with medication (if necessary)

Even if the pulmonary function is not altered due to training, strengthening of the respiratory musculature is expected as a training effect, long-term aiding in the reduction of the pulmonary function decrease after exercise and minimizing sedentarism, obesity and EIA effects[41-42].

CONCLUSION

The EIA mechanisms remain inconclusive; nevertheless, a physiological interaction involving the proposed theories seems to exist for the explanation of this phenomenon. The exercise test is an efficient device for EIA diagnosis if compared with bronchial reactivity tests induced by drugs such as methacholine and histamine. Concerning management, we highlight the importance of maneuvers such as the performance of pre-exercise warm-ups due to the refractory period as well as the utilization of beta-adrenergic substances for EIA prevention.

We also highlight the importance of physical activity practice for children and adolescents with EIA, since even if the exercise does not directly affect the pulmonary function, the reduction in sedentarism level as well as better quality of life derived from it justifies its regular application.

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