EXERCISE-INDUCED BRONCHOSPASM IN CHILDREN – NOT ALWAYS ASTHMA

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Abstract

Exercise-induced bronchoconstriction (EIB) is a dysfunction of the respiratory tract consisting of transient airflow obstruction that occurs during or immediately after physical exercise, being the preferred term to define what was known for years as exercise-induced asthma. Symptoms develop when airways narrow as a result of physical activity. As many as 90 percent of people with asthma also have EIB, but not everyone with EIB has asthma. EIB is defined as the coexistence of at least two of the following symptoms: dyspnea, cough, wheezing, shortness of breath and chest pain, combined with the decrease of forced expiratory volume in one second (FEV1). Perception of these symptoms may restrain children's ability and willingness to exercise. The pathophysiology of the process and the severity of bronchospasm depend on the level of ventilation, temperature and humidity of the inspired air. The mechanism is related to thermal hyperemia and congestion of small vessels in the bronchial wall. Most of the symptoms are non-specific, the differential diagnosis including chronic lung diseases and certain cardiovascular diseases or gastroesophageal reflux. For the diagnosis of this entity, a series of challenge tests can be used: at graded exercise, voluntary hyperpnea, methacholine, mannitol, hypertonic saline or histamine, FEV1 decreasing by 10-20% depending on the chosen test. Effective treatment includes preventive therapy - prior administration of a beta 2 agonist and/or antileukotriens, or regular CSI treatment in children with asthma that reduce the number of mast cells required for this type of response.

Key words: bronchospasm, effort, exercise, children

INTRODUCTION The temporary and reversible bronchoconstriction known as exercise-induced bronchospasm (EIB) can be experienced by people with or without asthma. It is characterized by expiratory dyspnea, wheezing, coughing, chest pressure, and mucus hypersecretion. Usually, it takes two to five minutes to manifest and dissapear within one hour after physical activity. The name "asthma," which was formerly in use, is debatable because physical activity causes bronchoconstriction in asthmatic patients but does not itself constitute a risk factor for the onset of asthma (1). The incredibly complicated chronic inflammatory disease known as asthma is brought on by an immune reaction that manifests as sporadic, reversible blockage of the lower airways in reaction to smooth muscle constriction due to an external stimulus, such as physical activity. It can be difficult to diagnose asthma in children because the diagnosis is primarily based on clinical criteria up until the age of five, or until the patient is able to demonstrate bronchospasm with a pulmonary function test (2). However, new research indicates that exercise, up to a person's personal tolerance, can prevent the occurrence of bronchial asthma in children (3).

EPIDEMIOLOGY

It is more common in high-performance athletes (up to 30%) and the pediatric population (3–35% in children under 16) than it is in the general population (5–20%). Urban children are 1.6 times more likely than rural children to have BIE, with socioeconomic status having little bearing on prevalence (4).

There are some minor differences between the risk factors and trigger factors for bronchial asthma and asthma attacks. The risk factors include: genetic or personal atopy; practicing winter or indoor sports; sports that require a high ventilation rate, such as skiing, football, marathon, hockey, swimming, or American football; exposure to irritants, such as aeroallergens, chloramine, pollutants, and intense exercise can also trigger asthma or the acute attack (5). The correlation between mouth breathing that prevents "heating the air" and chronic adenoiditis in children, which includes cold air entering the airways and causing bronchospasm, is also important to be taken into considerration. The attained level of ventilation, as well as the temperature and humidity of inspired air, determine the severity of exercise-induced bronchospasm; furthermore, the more severe the bronchospasm, the lower the temperature and higher the ventilation (6).

PATHOPHYSIOLOGY

It is basically unknown the pathophysiological pathway and the exact factors contributing to the occurrence of this entity. Among the triggers, hyperventilation during exercise results in heat loss and dryness in the airways, which raises intracellular osmolarity and causes cellular dehydration at this stage. Histamine, cytokines, leukotrienes, and other inflammatory mediators are released in response to the osmotic gradient that is produced. The onset of BIE is caused by an exaggerated local response brought on by these mediators and cellular dehydration. After the effort, a reactive hyperemia develops, which causes the osmotic gradient to change and new inflammatory mediators to be released, which lead to bronchospasm and local edema, while maintaining BIE (7). According to more recent research, breathing in large amounts of irritating particles or gases—such as chlorine from swimming pools or cold air from winter sports—rapidly can damage the respiratory epithelium. The appearance of hyperreactivity and bronchoconstriction is caused by damage to the epithelium, which results in local inflammation and the release of histamine, leukotrienes, and prostaglandins, as well as changes in the contractility of the bronchial smooth muscles. For example, changes in the contractile characteristics of airway smooth muscle and airway injury can lead to airway hyperresponsiveness in elite athletes (8).

The signs and symptoms of BIE are non-specific; in children, they include coughing, wheezing, chest pain, extreme fatigue, and decreased sports performance. These symptoms resemble those of asthmatic exacerbations, but they appear after five to ten minutes of vigorous physical activity. Crackles and wheezing may be heard during a clinical examination; however, these symptoms go away when the athlete rests. If an athlete exhibits wheezing while at rest, asthma will be diagnosed rather than BIE. Additionally, patients may exhibit symptoms of non-allergic or allergic diseases, contingent on the concomitant conditions (9).

DIAGNOSIS

Challenge tests are required for a definitive diagnosis. These include voluntary hyperpnea, graded effort, methacholine,

mannitol, hypertonic saline or histamine, and FEV1 decreasing by 10–20%, depending on the test selected, in children under the age of six, who are challenging to be evaluated (10).

Exercise Challenge Test: Spirometry is required to be evaluated at rest, for the first part of the test. The test should last eight minutes, with the first two minutes spent reaching 90% of maximum heart rate and the remaining six minutes spent maintaining this effort. With these parameters, most athletes can reach a sufficient level of ventilation (above 85% of maximum voluntary ventilation).

Mannitol challenge: it is not widely used, mostly because EU countries do not approve of this test, which causes muscle contraction by inducing the release of inflammatory mediators.

The methacholine challenge, which has been used to diagnose bronchial asthma has a low sensitivity for diagnosing BIE; nevertheless, a decline in FEV1 of more than 20% is regarded as positive (11) and baseline FeNO had a low predictive value for the development of EIB. This is consistent with a prior cross-sectional study conducted on athletes, which found that FeNO levels were not useful in differentiating between EIB-positive and EIB-negative participants. That is not the case, though, with research on kids and teens, where higher FeNO has been linked to verifiable proof of EIB. This is most likely caused in part by the various mechanisms that underlie EIB in the general public and in certain athletes. There is some explanation for the differences in FeNO and EIB results between athlete populations and the general population, as recent studies have shown distinct phenotypes of bronchial hyperresponsiveness and asthma in athletes, with a significant proportion of athletes having type 2 low inflammation (12).

When it comes to school-age children, differential diagnosis is crucial. Vocal cord dysfunctions (usually presenting with inspiratory wheezing and/or stridor) must be ruled out, as well as gastroesophageal reflux disease with unusual symptoms (children experiencing frequent regurgitation or vomiting), swimming-induced pulmonary edema (shortness of breath during or immediately following swimming with clinical signs of pulmonary edema, more common in male adolescents), and exercise-induced arterial hypoxemia (in children participating in competitive sports) (13).

Another condition that can mimic or exacerbate asthma is the paradoxical movement of the vocal cords, which are characterized by their adduction with airflow limitation. This condition is difficult to distinguish from asthma because it shares symptoms with wheezing, dyspnea, and cough, all of which are linked to stridor and hoarseness. The conditions that cause increased laryngeal sensitivity, such as respiratory infections, reflux, and posterior rhinorrhea, are the triggering factors. However, the development of this condition also has a psychopathological component, which attests to the critical role that the pediatric psychologist plays in the multidisciplinary medical team evaluating the pathology. Since the flow-volume curve and laryngeal exam are normal outside of attacks, diagnosis can be challenging. (14)

Digestive, respiratory, neurobehavioral, and non-existent symptoms are the different categories of GERD symptoms. Postprandial regurgitation and rumination syndrome in infants, vomiting,

dysphagia, and retrosternal or abdominal pain are among the digestive symptoms associated with GERD. The respiratory disorders can include recurrent otitis media, asthma, aspiration pneumonia, wheezing in infancy, pharyngitis, sinusitis, and chronic cough and laryngitis. Possible neurobehavioral manifestations of GERD include sleep disturbances, fits of agitation and crying, stiffness and arching of the neck, irritability, convulsions, and Sandifer syndrome in older children (15-18).

TREATMENT

1. Non-pharmacological treatment: low salt diet, antioxidants, fish oil, mask breathing, or just nasal breathing—all of which are challenging to achieve—as well as a sufficient warm-up prior to exercise. (19).
2. *Pharmacological treatment*
   - Short-acting β2 agonists: these should be taken into consideration as the preferred medication for preventing intermittent BIE in patients with and without asthma, particularly when used in conjunction with a sufficient warm-up prior to exercise. It is given 15 to 20 minutes before physical activity, preferably on a spacer (20).
   - In asthmatic athletes, long-acting β 2 agonists should only be used as a background drug in conjunction with CSI.
   - When given for four weeks before physical activity, CSI can lower BIE in adults with and without asthma as well as in children. In patients who are not asthmatic, long-term treatment did not significantly improve BIE prevention.
   - Leukotriene inhibitors work well for people with and without asthma diagnostic, especially in those with elevated IgE levels.

It is critical to determine the patient's capacity for participation in everyday activities because research has shown that, in the majority of cases, these activities require the administration of a preventive SABA before physical exercice, to avoid the bronchoconstriction they cause. A protective effect that is not present in the case of individuals treated regularly with inhaled corticosteroids (ICSs) is provided by a single dose of ICSs given to subjects who do not benefit from them as a background treatment. This protective effect reduces the frequency and severity of bronchoconstriction, without completely eliminating the need for acute therapy (21). As for uncontrolled, difficult-to-treat asthma and severe asthma, an appropriate evaluation is required in order to assure the right diagnosis and management. Before treatment step up, it is important to exclude an incorrect diagnosis, a poor adherence to treatment, incorrect inhaler technique or the presence of comorbidities. Treating associated comorbidities improves asthma outcomes as well. For example, children with asthma must be evaluated for gastroesophageal reflux in order to treat, as it can help the treatment of asthma or eliminating resistance to standard therapy (22).

Teenage patients deny the symptoms of their illness because they believe they are perfectly healthy. A young person's adolescent years are challenging because of peer and family pressure, as well as an underappreciation of the illness. Adolescents also attempt to follow in the footsteps of their peers by smoking cigarettes and engaging in risky behavior, which can lead to inadequate treatment, worsening of disease control, and

exacerbations of conditions. Furthermore, research indicates that bronchodilators (β2-agonists) are the most often prescribed medication for this group. Because of the anti-doping rules that limit athletes, this presents a number of issues. This is the reason some teenage patients might be reluctant to use this kind of treatment. However, some athletes have a tendency to abuse medication. As a result, bronchospasm management should also be provided to coaches, as well as athletes (23).

CONCLUSION

Exercise-induced bronchoconstriction is a condition that affects both asthmatic and non-asthmatic patients, but it affects performance athletes more frequently, particularly swimmers and those who engage in cold-weather sports. Provocation testing is required, as long as the diagnosis cannot be supported by anamnestic data or a clinical examination alone. In contrast to exercise-induced asthma, wherein inhaled corticosteroids are the preferred treatment option, short-acting β2 agonists and leukotriene inhibitors are the preferred treatments for exercise-induced bronchoconstriction.

AUTHOR CONTRIBUTIONS

M.M.A., I.M.S., A.M., E.H., L.P.A., C.P., I.T., S.N., T.C., I.D.M., A.N.A. contributed equally with I.K.I. to this article. All authors have read and agreed to the published version of the manuscript.

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