Review Article

Exercise-Induced Bronchoconstriction in Children and Adolescents

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Abstract: *Exercise-induced bronchoconstriction (EIB) is common in children. This article reviews the epidemiology, clinical presentation, pathophysiology, diagnosis, and treatment of EIB. EIB is caused by transient narrowing of the airways during or most often after exercise and indicates airway hyperresponsiveness. EIB is an important cause of exercise limitation in children. However, the diagnosis of EIB can be challenging because symptoms poorly predict the presence of EIB. Bronchial challenges, such as cardiopulmonary exercise testing, are required to document EIB. The severity of EIB is worsened by exposure to inhalational toxicants such as chlorine in pools and air pollution. In most children, EIB can be effectively prevented by both nonpharmacological means and medications. Educating the child, his/her family, and supervising adults about asthma triggers and management is important. Prompt recognition and treatment of an asthma attack associated with exercise is critical; bronchodilators should be on the sidelines at all times, and an asthma action plan should be in place.*

Keywords: asthma; exercise-induced bronchoconstriction; airway hyperresponsiveness; asthma management; medication therapy; lung function

The benefits of exercise are well known. Exercise improves conditioning, self-esteem,[1] and academic performance[2,3] and reduces cardiovascular disease and obesity.[4,5] In asthmatic individuals, exercise improves cardiopulmonary performance, fitness, breathlessness, and quality of life and decreases the need for asthma maintenance medications.[6,7] However, exercise is an important trigger for asthma attacks; it can cause bronchoconstriction. Exercise-induced bronchoconstriction (EIB) is caused by transient narrowing of the airways during or most often after exercise and indicates airway hyperresponsiveness.[8-11] EIB can be severe and can cause respiratory arrest and death.[12] EIB can be effectively treated and prevented. Therefore, it is extremely important to recognize the signs and symptoms of EIB.

This review is aimed toward delineating the epidemiology, clinical presentation, pathophysiology, diagnosis, and treatment of EIB in children and adolescents. EIB is an important cause of exercise limitation in children. Children are particularly at risk for EIB because they have higher rates of asthma than adults.[13] In addition, children are more active; approximately 30 million children and adolescents in the United States participate in organized sports.[14] The higher activity levels and relatively immature lungs of children may make them more susceptible to inhalational toxicants, such as air pollutants, which worsen EIB.[15-17] EIB in children can be effectively treated, and it is, therefore, important to recognize its signs and make an accurate diagnosis. However, in organized sports, children with asthma are often left in the care of coaches or supervising parents that have inadequate knowledge of their disease management.[18] Asthma education plays an important role in ensuring the optimal performance and safety of children with EIB.

Epidemiology

EIB occurs in 10% to 15% of children.[19,20] In children with persistent asthma, the prevalence of EIB is as high as 45% to 90%.[21-23] The prevalence increases with asthma severity and is greater in children with moderate or severe persistent asthma.[21] However, asthma severity does not necessarily correlate with the severity of EIB.[21] In children with asthma, EIB is considered to result from their underlying disease and is often referred to as exercise-induced asthma. However, EIB can also exist without any other evidence of persistent asthma.

Competitive endurance athletes, especially those who train in the cold weather,[24,25] indoor ice rinks,[21-25] and swimming pools,[26-28] have a particularly high risk of EIB without persistent asthma; 21% to 69% have EIB and airway hyperresponsiveness.[29-34] Studies on elite athletes include older adolescents. In those studies, female athletes seemed to have

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a higher prevalence than males.[35] The risk of EIB increases with the intensity of and amount of time spent training for the sport.[27,36,37] EIB improves when the athletes finish their competitive careers[36] or decrease their training intensity.[38]

Asthma and EIB are worse in children who play or exercise in high-pollution environments.[39-41] Exercise in the presence of air pollutants such as ozone, sulfur oxides, nitrogen oxides, and particulate matter is associated with EIB and pulmonary dysfunction.[42-44] In a study by McConnell and colleagues, the risk of developing asthma increased with the number of sports that children played in communities with high ozone levels. The relative risk increased over 3-fold in children who played 3 or more sports and increased if children played at least 1 high-activity sport.[16]

Sport-related asthma deaths do occur but are uncommon. Asthma was identified as the cause in only 1% of competitive athletes with sudden sport-related death.[12] In the study by Becker et al,[45] which reviewed asthma deaths associated with sports, approximately 80% of all deaths occurred in subjects younger than 21 years of age; half occurred in children between the ages of 13 and 17 years. Most were male (69%) and white (66%). This is in contrast to increased incidence of asthma deaths overall in blacks and Hispanics.[46] Many of the sports-related deaths occurred during practice (77%) and the remainder during games. In more than 90% of cases, there was a known history of asthma; however, only about 5% used maintenance medications such as inhaled corticosteroids and cromolyn.

Clinical Presentation

The symptoms of EIB include dyspnea or difficulty breathing, increased work of breathing, feeling "out of shape," chest tightness, shortness of breath, wheezing, chest congestion, and/or cough during or most often after exercise.[47,48] These symptoms are caused by narrowing of the airways, which produces increased airway resistance and obstruction to flow. EIB can be induced by short periods (6 minutes) of high-intensity exercise and occurs within minutes after the exercise is stopped. It usually resolves after 20 to 30 minutes. EIB is worsened by cold, dry air, air pollution, viral respiratory infections, and exposure to allergens.

Pathophysiology

The pathophysiology of EIB has not been completely understood. Exercise causes large increases in ventilation. The inspired air must be conditioned and humidified as it travels through the airways. This increase in airflow through the airways causes evaporative water loss, which results in increases in osmotic concentration (ie, drying) and thermal cooling.[11,49,50] The increase in osmolarity activates mast and epithelial cells to release inflammatory mediators, which leads to bronchoconstriction. Alternatively, EIB may be caused by changes in temperature and vascular tone in the airways. The increased airflow through the airways is associated with decreases in temperature. When the airways warm again after cessation of exercise, there is vasodilation, which may precipitate bronchoconstriction. Cold air provokes more severe EIB than warm air because of its lower humidity, which increases evaporative water losses. The resultant bronchoconstriction and inflammation causes increases in airway resistance and permeability and mucus production.

EIB is associated with atopy and inflammation, and it is more common and severe in allergic individuals.[51-53] Inflammatory mediators such as histamine, tryptase (from mast cells),[54] and cysteinyl leukotrienes[54,55] seem to play an important role in the pathogenesis of EIB. Eosinophils play an important role in the development of EIB; the severity of EIB correlates with eosinophilic inflammation[56] and elevated levels of exhaled nitric oxide (a noninvasive marker of eosinophilic inflammation).[57-59]

In endurance athletes, the high ventilatory rates attained with sustained aerobic exercise may injure the airway epithelium. The inflammation is further aggravated when the exercise is performed in cold weather. Moreover, the inhalational toxins and toxicants in the environment further increase the injury, for example, chlorine in pools, various air pollutants outdoors, and air pollution in indoor rinks produced by fossil-fuel-powered ice resurfacing machines.

Diagnosis

EIB should be suspected in children who present with exercise-induced respiratory symptoms. However, symptoms are often poor predictors of the presence of EIB.[48] In children with exercise-induced dyspnea, only 7% to 24% truly had EIB.[20,60-62] In college athletes, only 20% of those using bronchodilators had EIB.[63] On the other hand, there are also athletes who have "silent" EIB; in one study 36% of athletes without symptoms actually had EIB.[63]

There are many other possible causes of exercise-induced respiratory problems.[64] In a study by Abu-Hasan et al,[65] of 117 children with exercise-induced dyspnea, 9.4% has EIB, 41% had normal physiologic limitation, 22% had deconditioning, and 11% had vocal cord dysfunction (paradoxical movement of the vocal cords with exercise). Other less common findings included restrictive lung abnormalities (due to scoliosis or pectus excavatum), laryngomalacia, primary hyperventilation, and cardiac dysrhythmia. Though not specifically mentioned in the study, other potential causes of exercise-induced dyspnea include obesity and anxiety. The differential diagnosis also includes other uncommon diseases such as cardiomyopathy, aortic anomalies, pulmonary vascular disease, pulmonary arteriovenous malformation, exercise-induced hypoxemia, airway abnormalities, lung disease, and myopathy.[64]

Because of the difficulty of making the diagnosis of EIB by symptoms alone, it should be confirmed by standardized testing with spirometry and a formal challenge test. If spirometry reveals baseline obstructive pulmonary disease, then asthma should be suspected. Obstructive disease is indicated by a decreased ratio of forced expiratory volume in 1 second (FEV_1) to forced vital capacity often associated with a decreased FEV_1. A bronchodilator should be administered. If the FEV_1 increases

by 12% or greater, then, in the context of clinical symptoms, asthma can be diagnosed.[66] However, if spirometry is normal, then a challenge test is necessary to make the diagnosis of airway hyperresponsiveness. An exercise challenge test is used most often to recreate the symptoms that occur during exercise. Baseline spirometry is obtained. The child is then asked to exercise on a stationary bicycle or treadmill at 80% to 95% of his/her maximal heart rate for 6 minutes. Heart rate, respiratory rate, oxygen saturation, and blood pressure are monitored. Serial measurements of FEV_1 are obtained over the next 20 to 30 minutes. If the FEV_1 decreases by 10% or more, then EIB can be diagnosed.[67] In some exercise laboratories, the subject's level of conditioning can also be measured. Observation of the subject and information from the monitors can also yield important information such as hyperventilation, stridor (from vocal cord dysfunction or laryngomalacia), hypoxemia, or cardiac dysrhythmias.

A field test in the sports-specific environment can also be performed and may be more sensitive than laboratory tests; a decrease in FEV_1 of 15% or greater is required to diagnosis EIB.[68] Another test, eucapnic voluntary hyperpnea (EVH),[69,70] has also been used to assess for airway hyperresponsiveness.[56,57] The subject hyperventilates while breathing a 5% carbon dioxide mixture. Because the hyperventilation may be more than that achieved in a laboratory during exercise challenge, this test is also more sensitive for elite, conditioned athletes.[71] Inhaled powder mannitol has been recently introduced to assess airway hyperresponsiveness. The results of testing with inhaled mannitol correlate well with exercise testing and EVH.[72] Methacholine challenges have also been used to assess airway hyperresponsiveness. However, methacholine challenges do not correlate as well with exercise challenges or EVH.[73]

Treatment

Nonpharmacologic

A number of maneuvers are effective at decreasing EIB. Warm-up exercises, such as submaximal sprints, can decrease EIB.[74] Cooling down slowly after exercise may also help. Breathing primarily through the nose instead of the mouth during exercise protects against EIB; the nose and upper airway humidify the inspired air and decrease the evaporative losses in the lower airways.[75] The use of face masks in cold weather, particularly heat exchanger masks, effectively decrease EIB.[76-78]

Medications

The use of medications to prevent and treat EIB is effective. However, it must be emphasized that while medications may decrease the EIB response, they may not totally abolish it. Increasing ventilation by increasing the intensity of exercise or changes in the environment such as exposure to colder, drier air or air pollutants may overcome some of the protection.

In children and adolescents with persistent asthma, inhaled corticosteroids are the mainstay of preventative, anti-inflammatory therapy. Inhaled corticosteroids are the most potent and effective of the long-term control medications and improve EIB in a dose-dependent manner.[79-83] However, inhaled corticosteroids do not seem to be as effective in elite endurance athletes who have isolated EIB.[38] The lack of protection may be due to the epithelial injury and remodeling that endurance athletes sustain, which may not be as responsive to corticosteroids.

In asthmatics, combination therapy with inhaled corticosteroids and long-acting β2-agonists effectively controls asthma and EIB.[84] However, the use of long-acting β2-agonists has been associated with the development of tolerance and their effectiveness can wane over time.[85] In addition, the use of long-acting β2-agonists has been linked to an increase in asthma-related deaths.[86] Because of these findings, the US Food and Drug Administration and experts have recommended limiting the use of long-acting β2-agonists.[87,88]

Short-acting β2-agonists, therefore, are presently the therapy of choice for treatment of asthma exacerbations and EIB. They provide prompt relief, within 3 to 5 minutes, of bronchoconstriction. Short-acting β2-agonists are also effective at preventing EIB when given 15 to 30 minutes prior to exercise. Pretreatment with cromolyn and nedocromil also decrease EIB but are not as effective as β2-agonists;[75,76] they can be combined with β2-agonists for increased protection.[49] However, cromolyn and nedocromil are no longer available in the United States.[89] Antihistamines and topical steroid nasal spray may help decrease the severity of EIB.[90,91]

Montelukast offers protection against EIB.[92] While not as effective as β2-agonists, montelukast can be combined with them for enhanced protection.[93] Montelukast is not associated with tolerance.[94] Montelukast has proven to be effective against EIB when exercise is performed in the presence of high levels of particulate matter,[44] which may be particularly beneficial to athletes, for example, who train and/or compete in urban communities with many freeways and primary roads or in ice rinks with fossil-based resurfacing machines.

Management and Patient Education

Exercise should be encouraged in all children and adolescents with asthma. Exercise improves cardiopulmonary performance, fitness, and quality of life; it should be emphasized that it may also improve asthma control and decrease the need for maintenance medications.[6,7] Asthmatic athletes have the potential to perform optimally even at the elite level.[35] For instance, approximately 11% of the athletes on previous US Olympic Teams had asthma and/or EIB and they won as many gold medals as their nonasthmatic counterparts.[35,95]

To prevent EIB, athletes should be encouraged to perform warm-up and cool down exercises (see Table 1).[74] They should try to breathe primarily through their nose[75] and use face masks in cold weather.[76-78] Limitation of outdoor exercise on particularly frigid days should be considered, and possibly moving training indoors.

Measures to decrease exposure to air pollution during exercise are important.[96] The air quality index should be

Table 1. Exercise-Induced Bronchoconstriction: Educational Messages

Children can perform at elite levels if their asthma is adequately managed
Maneuvers can decrease EIB • Warm up before and cool down after exercise • Breathe primarily through the nose • Wear a mask on cold days
Outdoor and indoor air pollution may worsen EIB • Monitor outdoor air quality and alter training intensity, duration, or timing on poor air quality days • Avoid exercise close to high traffic areas • Assess and monitor air quality in indoor rinks or pools
Triggers such as viral upper respiratory infections, cold air, and inhalational allergens that may worsen EIB should be identified
Communication with the supervising adults, such as coaches, managers, and instructors, is important • Parents and children should inform supervising adults of the diagnosis and report all illnesses and limitations in activity • Children should be instructed to notify an adult if they develop symptoms of an asthma attack • An asthma action plan should be prepared for each child and communicated to the supervising adult(s)
Short-acting β2-agonists should be available on-site for both training and games • Correct technique with inhalers should be demonstrated

Abbreviation: EIB, exercise-induced bronchoconstriction.

monitored; an air quality index >50 reflects worsening air quality.[97] Outdoor exercise should be modified or limited in duration or intensity during days when air quality is poor,[98] and consideration should be given to moving training indoors. Exercise should be timed during early morning or evening hours when air quality is best. Exercise close to high-traffic areas should be avoided.[96]

For those who practice in indoor ice rinks or pools, education about the role of ambient air pollutants would be beneficial, and an assessment of the training environment should be performed. Both chlorine levels in pools and pollution levels—in particular carbon monoxide and nitrogen dioxide—in indoor rinks should be monitored.[99,100] Ventilation should be improved if levels are high. If the environment cannot be improved, then a change of venue should be considered, or else the duration and intensity of training may need to be limited.

It is important to identify triggers, such as cold air and viral upper respiratory infections, and inhalant allergens. Avoidance of allergens can improve asthma control, allergic rhinitis, and potentially EIB.[66] Identification of triggers by formal allergy testing may be necessary.[66] For example, for an individual with pollen or grass allergy, it is prudent to minimize exercise when the allergen levels are high.

Supervising adults on sports teams must be aware of which children have asthma and, therefore, may be at risk of an attack. Parents and children need to inform the supervising adults of any illness potentially influencing asthma control. Unfortunately, communication with coaches and managers is often inadequate, and children are left in the care of supervising adults who are unaware of which children have asthma or use bronchodilators and these adults may not have adequate knowledge about asthma treatment.[18] Asthma education should be an important part of the team leader training.

It is important to make sure that each team and child with asthma has an asthma action plan in the event of an acute attack. The early warning signs of an asthma attack should be reviewed with the child, his/her family, and supervising adults on the team. A child with known EIB who has difficulty breathing needs to understand that he/she should notify an adult. He/she should be immediately removed from the field of play and assessed. Two puffs of the short-acting β2-agonist should be given with attention to correct inhalational technique. Efforts should be made to keep the child calm, as anxiety may increase the dyspnea. If there is no improvement in 5 minutes, then the dose should be repeated. If there is still no improvement, then urgent care facilities should be notified, and the dose should be readministered until emergency medical services arrive.

Bronchodilators should be available at practice/training and game/competition facilities.[101] During an asthma attack, there is simply not always enough time to get to a medical facility, nurse's office, or backpack in a locker, before a respiratory arrest can ensue. Children who are cleared by their physicians and parents should keep the inhaler with them during school hours. Unfortunately, some athletic programs, even in the National Collegiate Athletic Association, do not ensure that bronchodilators are on the field for both practices and games.[102] Asthma education plays a key role in ensuring the optimal performance and safety of asthmatic children who exercise and participate in organized sports.

Conclusion

In children with asthma, an exercise program improves quality of life and fitness and decreases the need for asthma maintenance medications.[6,7,103] However, exercise can precipitate bronchoconstriction. The diagnosis of EIB cannot be made on the basis of symptoms alone; an exercise challenge or other bronchoprovocation test is necessary. EIB can be prevented with the use of both pharmacologic and nonpharmacologic measures. Effective treatment of EIB is necessary; respiratory arrest and death can ensue if it is not adequately managed. Education of the family and child about triggers and asthma management is crucial. Bronchodilators should be available on the sidelines during both practice/training and games/competition. Communication between the asthmatic child, his/her family, and supervising adults such as coaches, managers, and instructors is important. An asthma action plan should be in place for all asthmatic players. Asthma education should be an important part of team leader training.

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