

 **ISMJ**
International SportMed Journal

FIMS Position Statement 2011

Exercise-induced bronchoconstriction: Asthma in athletes

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Abstract

Exercise-induced bronchoconstriction (EIB) describes a condition of hyperpnea-triggered airway narrowing that occurs in susceptible individuals during or after physical exercise. The pathogenesis of EIB is multifactorial and not completely understood, but it seems that inflammation of the airways plays a major role. EIB is present in a large number of otherwise healthy athletes. Studies suggest that the prevalence in the athletic population ranges between 10 and 50%.

Key symptoms of EIB include dyspnea, cough, wheezing and chest tightness.

Pulmonary function tests with pharmacological (e.g. metacholine, carbachol, mannitol) or non-pharmacological (e.g. eucapnic voluntary hyperpnea) challenges are the principal diagnostic tools for the diagnosis of EIB.

The therapy for EIB involves preventive/non-pharmacological (e.g. warm up exercise, avoidance of triggers) and pharmacological (e.g. inhaled corticosteroids and β_2 mimetics) approaches. For the latter, the current anti-doping guidelines must be respected. **Keywords:** athlete, breathing, airway, bronchoconstriction

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Introduction

Exercise induced bronchoconstriction (EIB) describes a condition of hyperpnea-triggered airway narrowing that occurs in susceptible individuals during or after physical exercise. Several other terms, such as exercise induced asthma, exercise-induced bronchospasm or hyperpnea-induced airway irritability have been suggested to describe the same syndrome¹⁻³.

Due to the potentially negative impact on performance through impaired breathing and the strict regulations in the use of medication for the treatment of EIB, the diagnosis in athletes is of particular importance. In addition, athletes with EIB have a higher risk to develop upper respiratory tract infections and the condition is a risk factor for unexplained death in young healthy individuals. Accordingly, a high proportion of deaths in competitive athletes are asthma-related.

Epidemiology

EIB is present in nearly all asthmatics (~90%) and a large number of otherwise healthy athletes. Recent studies suggest that the prevalence in the athletic population ranges between 10- 50%. An accurate estimate remains nevertheless difficult, as prevalence studies use different diagnostic methods and criteria, and investigate different sporting disciplines, seasons, genders and environments. However, it can be summarised that the prevalence of EIB is higher in endurance athletes ("high-ventilation") than in strength-sport athletes ("low ventilation") and that it occurs more often in cold or hot and dry conditions than in moderate and humid environments. Other environmental aspects, such as the presence of potentially airway-irritating substances (chlorine for swimmers, ice-treating chemicals in figure skaters, speed skaters or ice hockey players, pollen for athletes with allergies) triggering the exacerbation of EIB have to be considered⁴⁻⁶. Finally, there are speculations that endurance athletes might develop EIB over time after many years of competitive sports, due to

chronic airway irritation caused by long-term, high-volume airflow in their respiratory system.

Pathogenesis

Several theories have been proposed to explain the hyperpnea-induced airway irritability. It is most likely multifactorial and not completely understood. A central aspect is that breathing large volumes of air within a short time causes an important evaporative water loss from the airway surface. This constitutes an osmotic and thermal stimulus in susceptible persons and triggers inflammation and subsequent bronchoconstriction through the release of mediators, such as histamine, leukotrienes and other inflammatory agents, causing a cough and mucus production⁷. It has to be pointed out that the role of inflammation on the pathogenesis of EIB is still subject to controversies, as the features of inflammations in non-asthmatic athletes with EIB are different to those observed in asthmatics.

Symptoms

Key symptoms of EIB include dyspnea, cough, wheezing and chest tightness. The condition might only present as a mild decrease in performance, fatigue or impaired recovery⁸.

Intensities of at least 80% of the individual maximal oxygen uptake ($VO_2\max$) are required to trigger the occurrence of EIB in most athletes. Symptoms can occur as early as 10 minutes after the onset of exercise, but usually peak ~10 minutes after the termination of exercise and can remain present for 30 minutes if no therapy is applied. After the cessation of symptoms, a refractory period of 2 to 4 hours with reduced reactivity of the airways is observed in certain athletes. During this time, these athletes are less prone to develop EIB symptoms.

Diagnosis

Pulmonary function tests with pharmacological or non-pharmacological challenge are the principal diagnostic tools for the diagnosis of



EIB. Tests should be carried out without prior use of medication affecting bronchoconstriction (β_2 -mimetics, inhalative corticoids). Changes in FEV1 are evaluated as follows (IOC Guidelines for the 2006 Winter Olympic Games)⁹:

Resting pulmonary function:

≥ 12% increase in the athlete's resting FEV1 after application of a bronchodilator by inhalation.

Non-pharmacological challenge:

≥ 10% decrease in FEV1 within 30 minutes after exercise (exercise test protocol: >85% of maximum heart rate for at least 4 min.)
≥ 10% decrease in FEV1 after eucapnic voluntary hyperpnea (EVH, 6 min breathing of dry air (5% CO₂, 21% O₂)).

Pharmacological challenge:

≥ 15% decrease in FEV1 after inhalation of a hypertonic aerosol (osmotic challenge, 22,5 ml of 4.5% saline).

≥ 20% decrease in FEV1 after inhalation of Metacholine (1-4 mg/ml or less).

Other pharmacological substances used to elicit EIB in pulmonary function tests include mannitol or carbachol. It has to be pointed out that tests using these substances are not recognised by the IOC for the diagnosis of EIB.

Comparative studies of various provocation techniques have shown that EVH has the highest specificity to unmask EIB in athletes^{10,11}.

Differential diagnosis

Other conditions limiting the airflow in the respiratory system have to be considered¹². The most common causes are listed in Table 1, together with their main difference to EIB.

Table 1: Differential diagnoses for EIB

Diagnosis	Main differences to EIB
Vocal Cord Dysfunction (VCD) Laryngeal/ tracheal processes Respiratory tract infection Gastro-oesophageal reflux Hyperventilation syndromes	Inspiratory wheeze, no response to β_2 mimetics Inspiratory wheeze, symptoms at rest Transient symptoms, other signs of infection No response to β_2 mimetics, proton-pump inhibitors help Different time line compared to EIB

Therapy

The therapy for EIB involves preventive/ non-pharmacological and pharmacological approaches.

Non-pharmacological therapy

Preventive measures should include full information of the athlete about the condition. Certain athletes might find that warming up intensively before exercise acts as a prophylaxis against subsequent EIB due to the phenomenon of the "refractory period". However, the refractory period has not been proven to be present in all athletes¹³. Other strategies to avoid the development of EIB include the avoidance of triggers (e.g. pollen), nasal breathing, and protection against cold/dry air by wearing a mask in cold environments.

Pharmacological therapy

Pharmacological therapy for EIB has been evaluated extensively. Although there is no general consensus on the best therapeutic

approach, it is generally acknowledged that inhaled corticosteroids and β_2 mimetics constitute the backbone of EIB therapy¹⁴. In particular, the addition of inhaled corticoids to the most commonly prescribed β_2 agonists might improve therapeutic success, as it usually reduces the frequency of β_2 mimetic application and prevents airway remodelling. Other substances that might be beneficial to some athletes include cromolyn compounds (for athletes with allergic dispositions) and leuktriene antagonists¹⁵.

For β_2 agonists, several problems have to be considered: Repetitive use of β_2 mimetics can trigger tachyphylaxis and desensitisation, and other side effects of this substance class are potentially harmful to the athlete (e.g. tachycardia, an increase in morbidity)¹⁶, especially if the correct dosage is exceeded, which is commonly observed in competitive settings.

Anti-doping



As several anti-EIB drugs are listed as prohibited substances by the World Anti-Doping Agency (WADA), any prescription of anti-asthmatic drugs to athletes should carefully be evaluated.

The following drugs/substance classes are allowed without restrictions:

- cromolyn derivatives
- leukotriene receptor antagonists
- theophyllines
- inhalative anticholinergic substances

Recently, WADA lifted restrictions on the use of inhalative glucocorticoids and certain (but not all) β_2 agonists (such as Salbutamol or Formoterol).

It has to be noted that there is compelling evidence that neither inhaled β_2 agonists nor inhalative glucocorticoids in therapeutic dosage improve sporting performance in non-asthmatic individuals. For this reason, the inclusion of these substances on the list of banned substances is continuously being discussed^{17,18}.

Summary

Exercise induced bronchoconstriction (EIB) affects 10-50% of all athletes. Air movement through the respiratory system, especially in high-ventilation sports, such as endurance events, results in relative drying and cooling of the airway wall with inflammatory and bronchoconstrictive responses. Symptoms of EIB include chest tightness, shortness of breath, wheezing and cough. Symptoms typically begin with a delay after the onset of exercise and peak after cessation.

Diagnosis is based on clinical symptoms and pulmonary function tests with pharmacological or non-pharmacological challenges. Eucapnic voluntary hyperpnea has been demonstrated to provide the highest sensitivity for this condition. Differential diagnosis for EIB includes vocal cord dysfunction, respiratory infections and gastro-oesophageal reflux disease.

The treatment of EIB is based on inhalative glucocorticoids and β_2 agonists; leukotriene antagonists and cromyl derivations might improve the treatment in certain athletes. As several drugs used in this context are banned by anti-doping regulations, careful scrutiny of the prohibited list of the World Anti-Doping Agency (WADA) is advised before prescription.

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