Exercise-Induced Bronchoconstriction – a Short Review with Practical Recommendations

Belastungsinduzierte Bronchokonstriktion – eine kurze Übersicht mit Praxisempfehlungen

Deputy Head, Division of Pneumology, University Hospital Freiburg, Freiburg

FRAUENLICHT

Summary: This article reviews the recent literature on exercise-induced bronchoconstriction (EIB) or exercise-induced asthma (EIA) and briefly summarizes the pathogenesis, diagnosis, and treatment of these conditions. Method: A literature research using PubMed, Medline and selective personal readings was performed to obtain articles on EIA and EIB. Summary: The term EIA covers exercise-induced symptoms and signs of asthma such as recurrent breathlessness, cough, wheezing, and chest tightness. EIB describes an expiratory obstructive reaction in lung function after a standardised exercise test. The pathophysiology of both diseases includes cooling of the airways, an increased loss of water from the respiratory tract and a relevant release of mediators from inflammatory cells of the airways, which could, on the long term, induce a chronically inflammatory response of the bronchi. The diagnosis of EIA or EIB includes the typical anamnesis and a positive exercise reaction or lung function testing with metacholine provocation. A eucapnic hyperventilation test, mannitol bronchial provocation or a field exercise test may be of help in some subjects. Data from the Olympic Games from 1996 until 2006 indicate a sport specific incidence of up to 20% amongst all athletes applying inhaled $\beta_2$-agonists with a verified diagnosis, emphasising on endurance disciplines. While diagnosing EIA / EIB numerous differential diagnoses have to be considered. Vocal cord dysfunction, poor physical fitness or overtraining are the most common. Therapeutically, adequate warm-up helps to reduce symptoms and inhaled corticosteroids or leukotrienreceptorantagonist are considered useful drugs for long term control and prevention. Supplementary, inhaled $\beta_2$-agonists are effective drugs for immediate inhibition of bronchoconstriction. Nevertheless, for all athletes the anti-doping regulations have to be applied. Further diagnostic evaluation should be considered if adequate treatment does not control the problem.

Key Words: Exercise-induced asthma, exercise-induced bronchoconstriction, athletes, vocal-cord dysfunction, inspiratory stridor.

Exercise. However, the pathophysiology is somewhat different. An ERS/EAACI-task force in 2008 defined that the term EIA should be used to describe symptoms and signs of asthma (such as recurrent breathlessness, cough, wheezing, and chest tightness) provoked by exercise and that EIB describes a reduction in lung function (obstructive expiratory flow limitation) after an standardised exercise test (6). These definitions were recently confirmed by the IOC and Wada committees favouring a broad comprehensive definition of these conditions in athletes (31,13).

accepted: September 2012
published online: November 2012
DOI: 10.5960/dzsm.2012.034
ÜBERSICHT

ße2-agonists (6). As expected, the usage of inhaled ß2-agonists was Olympic and 4.6% of the Summer Olympic participants used inhaled published data on the usage of inhalative drugs after application for cent asthmatic by Carlsen and Olympic athlete by Haathela (5, 14).

Methods

A medical literature research using PubMed, Medline and selective personal readings was performed to obtain articles on EIB. Search terms included: exercise-induced asthma, exercise-induced bronchoconstriction, athletes, vocal-cord dysfunction, inspiratory stridor. Only English and German publications were considered. It has to be emphasized that recently several societies and journals have published reviews in this field. This short review focuses mainly on the reports of the American Academy of Allergy, Asthma & Immunology Work Group from 2007 (32), the Joint Task Force of the European Respiratory Society (ERS) and the European Academy of Allergy and Clinical Immunology (EAACI) in cooperation with GA2LEN from 2008 (6, 7, 32) and the notable reviews on the breathless adolescent asthmatic by Carlsen and Olympic athlete by Haathela (5, 14).

Pathogenesis

The mechanism for development of EIA and EIB in athletes includes two hypotheses. Both relate to the increased ventilation of up to >200 L/min in elite athletes during exercise, resulting in an increased loss of water from the respiratory tract and cooling of the airways. This results in vasoconstriction of bronchial vessels followed by secondary reactive hyperemia, edema and airway narrowing (21). Furthermore, a relevant release of mediators from mast cells and other inflammatory cells of the airways, by changing the osmolarity of the periciliary fluid lining the respiratory mucosal membranes, can be measured (3). These mechanisms affect the course of EIA/EIB significantly, especially by inducing a chronically inflammatory response of the bronchial airways.

The classic early onset pattern reflects the signs of allergic asth- ma characterized by atopy, eosinophilic airway inflammation and positive methacholine responsiveness with a rapid onset of symp-toms at exercise initiation. The divergent pattern comprises a late onset phenotype during a sports career and therefore with more phases of high ventilation. Data on Finnish Olympic athletes support these findings and suggest these two different clinical phenotypes, which may reflect different underlying mechanisms due to the environmental conditions (14).

Problematic environmental conditions during the activity such as cold ambient temperatures for winter sports or organic chlorine products from indoor swimming pools clearly enhance the effect of intensive physical activity on both conditions. Especially swimmers, ice-hockey players, and cross-country skiers show a mixed type of eosinophilic and neutrophilic airway inflammation. Therefore, the inflammation may represent a multifactorial trauma, in which both irritant and allergic mechanisms play a role (14).

Prevalence

In general, exercise-induced asthma is a major problem for children and adolescents with known asthma bronchiale (20). Prevalence data of EIA/EIB among top athletes are conflicting due to methodological considerations. Most data for the prevalence of EIA or EIB in athletes were based on questionnaires without any attempts of clinical verifica-tion or other objective measures. Lung function based data with appropriate laboratory or field tests to verify or provoke respiratory symptoms (see figure 1). Typically, symptoms occur shortly after (sometimes during) intensive physical exercise with expira-tory dyspnea; regular rhonchi or wheezing may be observed by auscultation. A gradual improvement occurs either spontaneously or after usage of an inhaled bronchodilator (5, 25). The symptoms of asthma should be verified by the evidence of the reversibility of airflow obstruction or bronchial hyperreactivity confirmed by tests (5, 25) mentioned in Figure 1. It has to be considered, that there are athletes with mild BHR to medical stimuli who have negative ex-ercise challenges, but there are also individuals who have positive exercise challenges and negative histamine or methacholine chal-lenges (16, 18). These possibly conflicting test results may be due to the difference in mechanisms involved. In example, the above men-tioned late onset phenotype is more likely to respond to eucapnic hyperventilation tests (6). Additionally, a manitonal bronchial provo-ca tion or a field exercise test may be of help in some subjects (4).

If an exercise provocation is used, an ERS task force report on indirect airway challenges states the following recommendations: the subjects should exercise for six (children) to eight (adults) min at an intensity to raise the minute ventilation 14 times above the FEV1, and preferably to 21 times the FEV1 (60% maximum volun-tary ventilation) for the last four min of exercise. In the absence of a measure of ventilation the heart rate should achieve 90% predic-ted maximum in the last four min of exercise. Values for FEV1, are measured before and after exercise and a reduction in FEV1 of 10% of the pre-exercise value is widely accepted as outside the response observed in healthy individuals without asthma. Providing dry (and cold) air increase the severity of the airway response (18, 28).

Additionally, reversibility of airflow obstruction or BHR can also be confirmed by the measurement of airway resistance using bodyplethysmography as sometimes obstructions occur only in the central airways. However, there are no international threshold va-lue recommendations to confirm BHR in athletes, but an increase of more than 150% is generally accepted (9).

Diagnosis

The diagnosis of EIA/EIB requests the synthesis of medical history including details on respiratory symptoms, physical examination and appropriate laboratory or field tests to verify or provoke respiratory symptoms (see figure 1). Typically, symptoms occur shortly after (sometimes during) intensive physical exercise with expira-tory dyspnea; regular rhonchi or wheezing may be observed by auscultation. A gradual improvement occurs either spontaneously or after usage of an inhaled bronchodilator (5, 25). The symptoms of asthma should be verified by the evidence of the reversibility of airflow obstruction or bronchial hyperreactivity confirmed by tests (5, 25) mentioned in Figure 1. It has to be considered, that there are athletes with mild BHR to medical stimuli who have negative ex-ercise challenges, but there are also individuals who have positive exercise challenges and negative histamine or methacholine chal-lenges (16, 18). These possibly conflicting test results may be due to the difference in mechanisms involved. In example, the above men-tioned late onset phenotype is more likely to respond to eucapnic hyperventilation tests (6). Additionally, a manitonal bronchial provo-ca tion or a field exercise test may be of help in some subjects (4).

If an exercise provocation is used, an ERS task force report on indirect airway challenges states the following recommendations: the subjects should exercise for six (children) to eight (adults) min at an intensity to raise the minute ventilation 14 times above the FEV1, and preferably to 21 times the FEV1 (60% maximum volun-tary ventilation) for the last four min of exercise. In the absence of a measure of ventilation the heart rate should achieve 90% predic-ted maximum in the last four min of exercise. Values for FEV1, are measured before and after exercise and a reduction in FEV1 of 10% of the pre-exercise value is widely accepted as outside the response observed in healthy individuals without asthma. Providing dry (and cold) air increase the severity of the airway response (18, 28).

Additionally, reversibility of airflow obstruction or BHR can also be confirmed by the measurement of airway resistance using bodyplethysmography as sometimes obstructions occur only in the central airways. However, there are no international threshold va-lue recommendations to confirm BHR in athletes, but an increase of more than 150% is generally accepted (9).
Differential diagnosis
As described EIB symptoms typically occur shortly after (sometimes during) intensive physical exercise with expiratory dyspnoea (regular rhonchi, wheezing, cough) verified by the evidence of the reversibility of expiratory airflow obstruction or bronchial hyperreactivity confirmed by tests mentioned in Figure 1. Inhaled $\beta_2$-agonists are effective drugs for immediate inhibition of EIB (2). A failure to reduce the symptoms after ensuring a correct inhalation technique and adequate usage should direct to diagnostic considerations other than EIA or EIB. Although disorders affecting other organ systems enter into numerous differential diagnosis considerations, vocal cord dysfunction (VCD) is the most common and probably the most under diagnosed condition (8, 24, 25, 26). Here an abnormal adduction of the vocal cords leads to inspiratory airflow obstructions at the level of the larynx. VCD should be considered in subjects with inspiratory problems and / or stridor, an acute beginning of the respiratory problems (during (heavy) exercise) and a poor response to inhalative drugs; however, the definitive diagnosis can be made by direct rhinolaryngoscopy.

From an athlete’s point of view, lack of success in sports may also often be explained by minor respiratory complaints which are mistaken for asthma. Poor physical fitness or overtraining may represent possible differential diagnoses to EIA. This should especially be considered when the physical fitness and exercise performance are not up to the expectations of the athletes, trainers or parents (6,24). Among these two main differential diagnoses, several other differential diagnoses, such as exercise-induced arterial hypoxaemia and / or hyperventilation exist. It is therefore important for the diagnosis of EIA / EIB to perform a thorough examination, apparative examinations and to rule out other common differential diagnoses.

TREATMENT
EIA / EIB in athletes should be treated according to the same principles as in patients with asthma bronchiale. Adequate warm-up helps to reduce EIB (10,22,23) and inhaled corticosteroids (and / or leucotrienreceptorantagonist) are useful drugs for long term control and prevention (2,3,12,27). Supplementary, inhaled $\beta_2$-agonists are effective drugs for immediate inhibition of EIB (2). It should be emphasized that the overuse of short and long acting bronchodilators ($\beta_2$-agonists) leads to tolerance and may have significant detrimental effects on health (17,24). Since 2012 all $\beta_2$-agonists are prohibited for competitive athletes except salbutamol (maximum 1600µg over 24h), formoterol (maximum 36µg over 24h) and salmeterol when taken by inhalation (31). All $\beta_2$-agonists (e.g. terbutaline, procaterol) not mentioned as exceptions above are prohibited and require a Therapeutic Use Exemption (TUE), with exception of clenbuterol, which is generally forbidden (31,30).


Correspondence: Prof. Dr. med. Stephan Sorichter University Hospital Freiburg Division of Pneumology Kilianstr. 5 79102 Freiburg E-Mail: stephan.sorichter@uniklinik-freiburg.de