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EXERCISE-INDUCED BRONCHOCONSTRICTION: PATHOGENESIS, SYMPTOMS, DIAGNOSIS AND CURRENT TREATMENT - LITERATURE REVIEW

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ABSTRACT

Objective: Exercise-induced bronchoconstriction (EIB) is a reversible narrowing of the airways that occurs during or shortly after physical exertion, affecting both individuals with asthma and those without prior respiratory diagnoses. EIB is particularly prevalent among athletes and individuals exposed to cold, dry air or environmental pollutants. This article aims to present an updated review of EIB, focusing on its underlying mechanisms, clinical symptoms, diagnostic approaches, and current treatment options.

Methods: A comprehensive review of recent literature was conducted, examining the pathophysiology, clinical manifestations, diagnostic criteria, and management strategies of EIB. The search incorporated studies addressing both pharmacological and non-pharmacological interventions, as well as diagnostic methodologies such as spirometry and bronchial provocation tests.

Key findings: EIB primarily results from airway dehydration and cooling during exercise, triggering the release of inflammatory mediators like leukotrienes and prostaglandins that cause bronchoconstriction. Patients typically experience symptoms including shortness of breath, wheezing, cough, and chest tightness, which can severely impact exercise performance and quality of life. Diagnosis is best established through objective lung function testing, with a fall in FEV1 by 10% or more after exercise being indicative of EIB. Inhaled short-acting β2-agonists remain the cornerstone of treatment, while inhaled corticosteroids and leukotriene receptor antagonists serve as adjunct therapies in cases with underlying asthma or persistent symptoms.

Conclusions: Accurate diagnosis and tailored management are essential to enable individuals with EIB to engage safely in physical activities. Combining pharmacological treatments with lifestyle modifications provides effective symptom control. Ongoing research is warranted to refine diagnostic tools and optimize therapeutic protocols to further improve outcomes for affected individuals.

KEYWORDS

Exercise-Induced Bronchoconstriction, Exercise-Induced Asthma, EIB, Asthma, Bronchoconstriction

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Introduction

Exercise-induced bronchoconstriction (EIB) is a respiratory condition that manifests as an acute narrowing of the airways. It can occur during or after physical activity.

EIB affects approximately 5-20% of people without a prior diagnosis of asthma and up to 90% of those with diagnosed asthma. [1, 2] It is frequently observed in otherwise healthy athletes, particularly those exposed to cold, dry air or airborne pollutants during training and competition. [3]

It is noteworthy that higher prevalence rates can be observed among individuals who train in endurance sports. [4, 5]

The pathophysiology of EIB is not yet fully understood and involves molecular and cellular mechanisms. [6, 7] Two main theories are frequently cited to explain the development of EIB: the osmotic and thermal theories, which relate to airway cooling and dehydration during exercise. [8, 9] Physical exertion induces increased levels of histamine, leukotrienes and prostaglandins, which cause increased bronchospasm.

It is now recognised that both environmental and genetic factors contribute to EIB susceptibility, with atopy, respiratory infections, and urbanization identified as additional risk factors, especially in children and adolescents.

EIB most often presents with shortness of breath, wheezing, cough, and chest tightness.

Less typical symptoms can include headache, abdominal pain, muscle cramps, dizziness, and fatigue. [10]

Exercise-induced bronchospasm has a significant impact on the quality of life of patients, especially those with asthma. The symptoms they experience significantly increase feelings of anxiety and frustration compared to asymptomatic individuals. [4, 11] Athletes affected by EIB may perform worse in competitions, and their training may be less effective.

Diagnosis of EIB relies primarily on objective testing through spirometry and bronchial provocation tests, as symptoms alone are unreliable predictors of the condition. [2, 12]

The American Thoracic Society guidelines recommend exercise challenge testing combined with dry air inhalation, with a positive test defined as a ≥10% decrease in forced expiratory volume in one second (FEV1) from baseline. [12] However, owing to low awareness of EIB and lack of standardized diagnostic methods, under-diagnosis and mis-diagnosis remain common problems in clinical practice. [13] Studies demonstrate that up to 86% of EIB-positive athletes have no prior history of the condition or asthma, highlighting the substantial burden of undiagnosed disease. [14]

Current treatments include both pharmacological and non-pharmacological interventions, and management strategies vary depending on whether EIB occurs with clinical asthma or in healthy individuals. First-line therapy is short-acting β2-agonists (SABAs) used prior to exercise. When asthma control is suboptimal, inhaled corticosteroids and leukotriene receptor antagonists are recommended. Non-pharmacological measures include warm-up routines and trigger avoidance. [15]

There has been increased interest in complementary approaches, including nutritional interventions that target inflammatory processes and airway smooth muscle function. [13]

Given the high prevalence of EIB in various populations and its significant impact on physical activity and quality of life, a comprehensive understanding of this condition is essential for respiratory and sports medicine professionals.

Methodology

This narrative review was conducted by systematically searching the PubMed and Google Scholar databases to identify relevant literature on exercise-induced bronchoconstriction.

The search terms included”exercise-induced bronchoconstriction, ”“exercise-induced asthma, ”“EIB, ”“asthma in athletes, ”“pathophysiology, ”“diagnosis, ” and”treatment.” Articles published in English, focusing on studies from recent decades, were considered.

The inclusion criteria encompassed original research articles, clinical guidelines, reviews, and meta-analyses that addressed the mechanisms, clinical presentation, diagnostic methods, and management of EIB. Data extraction focused on synthesizing evidence regarding the underlying pathophysiology, symptomatology, objective diagnostic criteria, and both pharmacological and non-pharmacological therapeutic interventions.

The analysis prioritized studies demonstrating clinical relevance and applicability to both general and athletic populations. This approach aimed to consolidate current evidence and identify gaps for future research in the field of exercise-induced bronchoconstriction.

Pathogenesis

The pathogenesis of exercise-induced bronchoconstriction is multifactorial, with two main theories being recognised as the main mechanism: the osmotic and thermal hypotheses. [8, 9, 16]

The osmotic theory explains that high-intensity ventilation during exercise leads to evaporative water loss from the airway surfaces, resulting in increased osmolarity of the airway lining fluid. This hyperosmolar environment triggers mast cell degranulation and the release of the inflammatory mediators such as histamine, prostaglandins, and leukotrienes. [17] It results in bronchial smooth muscle contraction, increased mucus secretion and microvascular leakage, collectively leading to bronchoconstriction. [18]

The thermal theory suggests that inhalation of large volumes of cold air during the exercise causes cooling of the airway mucosa. When exercise ceases, rapid rewarming leads to reactive hyperemia and increased bronchial blood flow, resulting in vascular leakage and bronchoconstriction. [19]

These mechanisms are not mutually exclusive and may act synergistically, especially in athletes exercising in cold or dry environments.

Repetitive cycles of airway dehydration and rehydration can cause epithelial injury and heightened airway hyperresponsiveness. [20]

Recent research highlights that airway epithelial damage is not only a consequence of repeated dehydration but also of exposure to environmental irritants such as pollutants, allergens, and chlorinated water, which are particularly relevant for swimmers and urban athletes. [21, 22]

It has been demonstrated that release of inflammatory mediators during EIB episodes can lead to chronic changes in airway structure, including subepithelial fibrosis, and increased smooth muscle mass, especially in individuals with frequent or severe symptoms. [23]

Genetic predisposition, atopy, and a history of respiratory infections have also been identified as factors that may increase susceptibility to EIB, suggesting a complex interplay between environmental exposures and individual biological characteristics. Genome-wide association studies and clinical observations indicate that individuals with a family history of asthma or atopic diseases are at higher risk for developing EIB. [24]

Furthermore, studies using advanced imaging and biomarker analysis have revealed that airway hyperresponsiveness in EIB is associated with increased permeability of the airway epithelium and upregulation of pro-inflammatory cytokines, such as IL-8 and TNF-α, supporting the role of both innate and adaptive immune responses in the pathogenesis of this condition. [25, 26]

Symptoms

The clinical presentation of exercise-induced bronchoconstriction (EIB) is characterized by transient respiratory symptoms that typically manifest during or shortly after physical exertion, with peak intensity occurring 5-15 minutes post-exercise and spontaneous resolution within 60 minutes in most cases. [16, 17]

Core symptoms include dyspnea, wheezing, cough, and chest tightness or pain, which collectively arise from acute airway narrowing and inflammatory mediator release. [19]

Wheezing is particularly notable during exhalation due to turbulent airflow through constricted bronchi, while cough often presents as persistent and non-productive.

Less common but clinically significant atypical symptoms include headache, fatigue, abdominal pain, muscle cramps, dizziness, and generalized fatigue.[8]

It is important to emphasize that the severity of symptoms does not always correlate with the degree of bronchoconstriction measured objectively, which can lead to both underestimation and overestimation of the condition in clinical practice. [27]

Some individuals may experience only subtle manifestations, such as a sensation of being out of shape, mild chest discomfort, or unexplained fatigue, which may delay diagnosis and appropriate management.

In children and adolescents EIB can present with behavioural changes, avoidance of physical activity, or decreased participation in sports, which may be mistakenly attributed to lack of motivation or poor fitness. [28, 29]

Notably, symptoms alone lack diagnostic specificity, as up to 86% of athletes with objectively confirmed EIB report no prior respiratory complaints. [30, 31]

The transient nature of symptoms contributes to underreporting. Many individuals normalize symptoms as an inevitable consequence of intense exercise rather than seeking evaluation.

Diagnosis

The diagnosis of exercise-induced bronchoconstriction (EIB) necessitates objective testing due to the poor specificity of symptoms such as dyspnea, cough, or wheezing, which overlap with other conditions like exercise-induced laryngeal obstruction, cardiac issues, or physical deconditioning. [13, 31]

Spirometry remains the cornerstone of diagnosis, with the American Thoracic Society guidelines defining a positive test as a ≥10% decrease in forced expiratory volume in one second (FEV1) following an exercise challenge. [1] The exercise challenge test typically involves 6-8 minutes of high-intensity exercise (targeting > 85% maximum heart rate) in dry air conditions, followed by spirometry at 5, 10, 15, and 30 minutes post-exercise to capture the peak bronchoconstrictive response. [1, 31]

For populations where standard exercise testing is impractical, bronchoprovocation tests like eucapnic voluntary hyperpnea (EVH) or inhaled mannitol offer alternatives. [32]

EVH simulates exercise-induced hyperventilation using dry air/gas mixtures. [33]

Mannitol challenge, which induces osmotic airway changes, requires a ≥15% FEV1 decline for positivity. [31]

Pre-test medication management is essential to avoid false negatives. Current guidelines mandate withholding short-acting β2-agonists (SABAs) for ≥8 hours and long-acting β2-agonists (LABAs) for 36 hours before testing. [1, 34]

For athletes, diagnostic challenges are compounded by high rates of undiagnosed EIB - studies indicate that the majority of EIB-positive athletes lack prior symptoms or asthma history, emphasizing the need for proactive screening in high-risk groups. [35]

Advanced diagnostic approaches, including the use of exhaled nitric oxide measurement and airway inflammation biomarkers, are being explored to improve diagnostic accuracy and to help differentiate EIB from other causes of exertional dyspnea. [36, 37]

It is also important to distinguish EIB from conditions such as exercise-induced laryngeal obstruction, vocal cord dysfunction, and cardiac or psychological causes of breathlessness, as these may require different management strategies.

Screening for EIB in high-risk groups, such as swimmers, skiers, and endurance athletes, has been proposed to facilitate early detection and intervention, although the cost-effectiveness and practicality of widespread screening remain under investigation. [38]

Underdiagnosis persists due to limited access to standardized testing and low clinical awareness, particularly in primary care.

Treatment

The management of exercise-induced bronchoconstriction (EIB) requires a multifaceted approach that integrates pharmacological and non-pharmacological strategies tailored to the patient's clinical profile, including asthma status, symptom severity, and athletic demands.

Pharmacological interventions remain foundational, with inhaled short-acting β2-agonists (SABAs) such as albuterol serving as first-line therapy when administered 15-30 minutes pre-exercise. [16]

However, daily SABA use risks tachyphylaxis and diminished efficacy, necessitating limitation to ≤ 3 weekly doses for prophylaxis.

For patients with persistent symptoms or underlying asthma, inhaled corticosteroids (ICS) are recommended to mitigate airway inflammation and hyperresponsiveness, with optimal effects emerging after 2-4 weeks of consistent use.

Leukotriene receptor antagonists (LTRAs), such as montelukast, provide an alternative for SABA-resistant cases.

Non-pharmacological strategies are equally critical. Pre-exercise warm-up routines involving high-intensity intervals followed by moderate activity induce a 1-2 hour refractory period and reduce FEV1 decline. [39]

Environmental adaptations - such as avoiding cold and dry air, using face masks for air humidification, and minimizing exposure to pollutants - decrease symptom severity. [34]

Recent guidelines emphasize the importance of individualized treatment plans, taking into account comorbidities, environmental exposures, and the specific demands of the patient's sport or activity.

There is growing evidence that combining pharmacological and non-pharmacological interventions yields superior symptom control and allows for greater participation in physical activity without compromising respiratory health. [40, 41]

Adjunctive therapies, such as anticholinergic agents or biologics targeting specific inflammatory pathways, are being explored for patients with refractory EIB or coexisting severe asthma, although their use remains limited to select cases. [42]

Emerging evidence supports nutritional interventions, including omega-3 fatty acid supplementation, which reduces inflammatory mediator release. [43, 44]

Dietary modifications, such as increasing antioxidant intake and maintaining optimal vitamin D levels, have also been proposed to support airway health and reduce EIB severity, though further research is needed to confirm their efficacy.

For athletes, treatment must align with World Anti-Doping Agency (WADA) regulations: inhaled SABAs and ICS are permitted via Therapeutic Use Exemption (TUE). [16] Athletes with frequent exercise exposure may benefit from combination therapy, like ICS paired with formoterol. [15]

Patient education on trigger avoidance, adherence, and inhaler technique is paramount. Ongoing support and education can improve treatment adherence, reduce the risk of exacerbations, and empower patients to self-manage their condition effectively.

Long-term management should address airway remodeling risks in elite athletes, where untreated EIB correlates with subepithelial fibrosis. Regular follow-up, every 6-12 months, with spirometry and symptom assessment ensures therapy optimization and prevention of irreversible airway changes. [45]

Discussion

The findings reviewed in this article emphasize the critical importance of recognizing exercise-induced bronchoconstriction (EIB) as a distinct clinical entity that significantly affects both athletes and the general population. The elucidation of underlying mechanisms, primarily airway dehydration and cooling leading to inflammatory mediator release, highlights key targets for intervention. These insights have substantial implications for improving diagnostic accuracy, as symptom-based assessments alone are insufficient and often result in underdiagnosis, particularly in high-performance athletes.

The reliance on objective pulmonary function testing, including spirometry and bronchial provocation, is essential to confirm EIB and guide appropriate therapy.

From a therapeutic perspective, the evidence supports an integrated approach combining pharmacological treatments such as pre-exercise short-acting β2-agonists and inhaled corticosteroids with non-pharmacological measures like warm-up exercises and environmental modifications. This multidisciplinary strategy not only controls acute symptoms but also reduces the risk of chronic airway changes and preserves athletic performance. Moreover, awareness of underdiagnosis underscores the need for education among clinicians, coaches, and patients to promote timely identification and adherence to management plans.

Overall, this review underscores that advancing both screening practices and personalized treatment protocols will enhance quality of life for individuals affected by EIB.

Continued research should focus on refining diagnostic methods, exploring novel therapeutic options, and understanding the long-term consequences of EIB in various populations.

Such efforts will contribute to optimizing care and supporting ongoing physical activity without compromising respiratory health.

Conclusion:

Exercise-induced bronchoconstriction (EIB) is a manageable condition requiring integrated pharmacological and non-pharmacological strategies for optimal control. Pharmacological interventions like pre-exercise short-acting β2-agonists and inhaled corticosteroids effectively prevent acute symptoms, while non-pharmacological approaches, like warm-up routines, trigger avoidance, and environmental modifications significantly reduce symptom severity. Accurate diagnosis through objective testing is essential, especially in athletes where underdiagnosis is prevalent. Collaborative care involving clinicians, coaches and patients ensures personalised management and adherence. With appropriate treatment and monitoring, individuals with EIB can maintain unrestricted physical activity and athletic performance without compromising respiratory health.

Disclosure

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Software - Kamil Marzec, Anna Hawryluk
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