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The Diagnostic Value of Exercise Bronchial Provocation Testing in Pediatric Asthma

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ABSTRACT

Objective: Exercise-induced bronchoconstriction (EIB) is characterized by transient airway narrowing that occurs during or after physical activity. While it is commonly observed in individuals with asthma, it can also be seen in otherwise healthy children and adolescents. Exercise bronchial provocation tests are among the primary diagnostic tools used to assess EIB. This study aimed to investigate the relationship between the frequency of EIB and the diagnosis of asthma in pediatric patients who underwent exercise bronchial provocation testing.

Materials and Methods: Pediatric patients who underwent exercise bronchial provocation testing at the Pediatric Allergy and Immunology Clinic of Ankara Bilkent City Hospital between October 2023 and October 2024 were retrospectively evaluated. Demographic data, clinical symptoms, spirometric measurements, allergen sensitization status, and final diagnoses were obtained from medical records. A decrease in FEV1 of ≥10% from baseline was considered diagnostic for EIB.

Results: Among the 79 patients included in the study, 59.6% were female, with a median age of 14.5 years (IQR: 12-16). A positive exercise bronchial provocation test was observed in 54 patients (68.4%). Of these, 44 were diagnosed with EIB associated with asthma (EIBa), and 10 were diagnosed with exercise-induced bronchoconstriction without asthma (EIBwa). Despite a negative exercise provocation test, clinical evaluation revealed symptom patterns consistent with asthma in 7 patients, leading to a confirmed diagnosis. The positive predictive value for asthma diagnosis was 81.5%, and the negative predictive value was 72%. Allergic rhinitis was identified in 21 patients, 18 of whom had EIB, and aeroallergen sensitization was present in 37.0% of those with EIB.

Conclusion: Exercise bronchial provocation testing is a useful tool for evaluating exercise-induced respiratory symptoms, and its diagnostic value increases when correlated with clinical findings and allergologic assessment, particularly in the context of suspected asthma. Further studies are needed to clarify its role in pediatric practice.

Keywords: Asthma, exercise-induced bronchoconstriction, pediatric

INTRODUCTION

Exercise-induced bronchoconstriction (EIB) refers to transient narrowing of the airways that occurs during or after intense physical activity. It is common among individuals with asthma who frequently experience respiratory symptoms such as cough, wheezing, chest tightness, and excessive mucus production. However, EIB can also occur in otherwise healthy individuals, including children, adolescents, and those who engage in regular physical exercise (1,2).

Exercise is widely recognized as a trigger of acute asthma exacerbations. The term 'exercise-induced asthma', introduced about sixty years ago, initially described exercise-related respiratory symptoms, including transient bronchoconstriction. However, it inaccurately implied that exercise was the primary cause of asthma attacks.

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To clarify this, the term 'exercise-induced bronchoconstriction' was later adopted. In the early 2000s, an international consensus formally distinguished between EIB in individuals with underlying asthma and EIB in those without asthma, in whom no other asthma-related signs are present (1,3).

EIB primarily results from the loss of airway water due to increased ventilation during physical exertion, leading to airway dehydration and hyperosmolarity. This hyperosmotic environment triggers the release of inflammatory mediators such as histamine, leukotrienes, and prostaglandins from mast cells and eosinophils, causing bronchial smooth muscle contraction and airway narrowing. Additionally, airway cooling followed by rapid rewarming during exercise may exacerbate bronchospasm through vagally-mediated reflexes and neurogenic inflammation (4). EIB reportedly typically occurs within 2-5 minutes after exercise, peaks after 10 minutes, and resolves in approximately 60 minutes. Exercise bronchial provocation tests represent a standard diagnostic tool for EIB, enabling the direct evaluation of airway responsiveness (3,5).

The aim of this study was to evaluate the presence and severity of exercise-induced bronchospasm in pediatric patients who underwent exercise provocation testing, and to examine its association with a diagnosis of asthma.

MATERIALS and METHODS

Study Design

Between October 2023 and October 2024, patients who underwent an exercise provocation test at the Pediatric Allergy and Immunology Department of Ankara Bilkent City Hospital were retrospectively evaluated.

Presenting symptoms, exercise-related complaints (such as cough and dyspnea), diagnoses, therapeutic interventions, and treatment outcomes were extracted from the hospital's electronic medical records and systematically recorded using standardized data collection forms routinely employed by pediatric allergy and immunology specialists.

Spirometry

Pulmonary function tests (PFTs) were conducted using a portable dry-flow volumetric spirometer (MiniSpir®, MIR - Medical International Research, Rome, Italy) in accordance with established protocols. Spirometry assessments adhered to the guidelines of the American Thoracic Society (ATS) and the European Respiratory Society (ERS) (6). Study participants were seated in the upright position; at least three acceptable maneuvers were obtained and the best forced expiratory volume 1 (FEV1) was used. Testing equipment was calibrated daily to ensure accuracy and precision.

Exercise Challenge Test

Exercise challenge testing was performed in children presenting with exercise-related respiratory symptoms, including exertional cough, chest tightness, or dyspnea.

The exercise challenge test was conducted in accordance with the ERS. The protocol included a treadmill based running exercise lasting 6 to 8 minutes, aiming to reach 80-90% of the predicted maximum heart rate. Spirometric measurements were obtained at baseline and at 5, 10, 15, and 20 minutes post-exercise. A decrease in FEV1 of ≥10% from baseline was considered diagnostic for EIB. In preparation for the test, patients were instructed to withhold short-acting bronchodilators for 8 hours and to discontinue long-acting bronchodilator/inhaled corticosteroid combination therapies 36 hours prior to the procedure, in accordance with standard recommendations (7).

Patients were classified according to their clinical presentation and the results of the exercise challenge test. Those with a positive test for exercise-induced bronchoconstriction (≥10% fall in FEV1) and whose symptoms and clinical findings were consistent with asthma (such as recurrent wheezing, cough, or response to controller therapy) were classified as exercise-induced bronchoconstriction with asthma (EIBa), patients with a positive test but without clinical features suggestive of asthma, and whose symptoms occurred exclusively during exercise, were classified as exercise-induced bronchoconstriction without asthma (EIBwa) (1,3).

A diagnosis of asthma was established in patients with supportive clinical features and/or a significant bronchodilator response, defined as an increase in FEV1 of more than 12% following administration of a short-acting bronchodilator (8).

Patients reporting chest pain prior to undergoing the exercise bronchial provocation test were initially referred to the cardiology department for cardiac assessment, including electrocardiography and, when indicated, echocardiography.

Atopy

Patients underwent skin-prick-tests for common inhalant allergens including animal dander, house dust mite, mixed tree and mixed grass pollen, and mold (Lofarma, Milan, Italy). Saline solution (0.9% sodium chloride) and histamine hydrochloride are used as negative and positive controls, respectively. Results were evaluated 15-20 minutes after application. An induration at least 3 mm in diameter surrounded by erythema was considered a positive result. Serum-specific IgEs were used for in vitro tests (Siemens Immulite, 2000).

Ethics

We received approval from the Clinical Research Ethics Committee of Ankara Bilkent City Hospital (Ethical approval number: TABED 2-25-1138). The study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from the parents or legal guardians, and from children over 9 years of age, prior to performing the exercise bronchial provocation test.

Statistics

Data from medical records were analyzed using the IBM Statistical Package for the Social Sciences version 26.0 (SPSS Inc., Chicago, IL, USA). Descriptive data were given as 25 and 75 percentiles interquartile range (IQR). Categorical variables were presented as frequencies (n) and percentages.

RESULTS

Exercise Bronchial Provocation Tests

A total of 79 patients who underwent exercise bronchial provocation testing were included in the study. A positive test response, defined as a ≥10% decline in FEV1, was identified in 54 patients (68.4%), whereas 25 patients (31.6%) exhibited a negative response. Among those with a positive test, 44 patients were diagnosed with EIBa, and 10 patients with EIBwa. Despite a negative exercise provocation test, clinical evaluation revealed symptom patterns consistent with asthma in 7 patients, leading to a confirmed diagnosis (Figure 1). Exercise bronchial provocation testing demonstrated a median decrease in FEV1 of 12% (IQR: 8-16%).

The positive predictive value (PPV) of the exercise bronchial provocation test for asthma diagnosis was 81.5%, and the negative predictive value (NPV) was 72%.

Demographic and Clinical Characteristics of the Study Subjects

The median age of the patients was 14.5 years (IQR: 12.0-16.0), and 45 (57%) were female. Concomitant allergic rhinitis was present in 21 (21/79, 26.5%), of whom 18 (18/54, 33.3%) had a positive exercise bronchial provocation test. A total of 25 patients (25/79, 31.6%) had aeroallergen sensitization. Among these patients, 20 were found to have a positive exercise bronchial provocation test, rep-

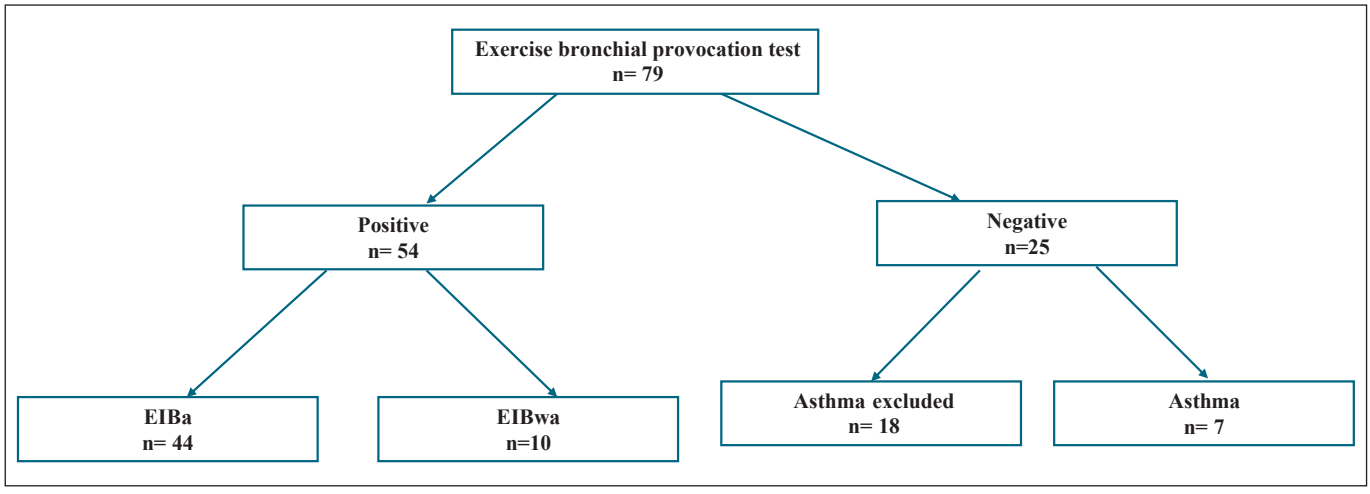

Figure 1: Flow chart of patients who underwent exercise bronchial provocation testing.
EIB: *Exercise induced bronchoconstruction,* ***EIBa:*** *Exercise induced bronchoconstruction with asthma,* ***EIBwa:*** *Exercise induced bronchoconstruction without asthma*

Table I: Clinical and laboratory characteristics of the patients

Characteristics	n=79 (%)
Age, year, median (IQR)	14.5 (12.0-16.0)
Female	45 (56.9)
Concomitant allergic rhinitis	21 (26.5)
Aeroallergen sensitization	25 (31.6)
Pollen	18 (22.7)
House dust mites	13 (16.5)
Cat	2 (2.5)
Mold	1 (1.3)
Cockroach	1 (1.3)
Presenting symptom	
Exertional dyspnea	75 (94.9)
Exertional cough	64 (81)
Nocturnal cough	38 (48.1)
Non-exertional cough	34 (43)
Treatment	49 (62.0)
Maintenance inhaled corticosteroid and long acting beta agonist	30 (61.2)
Maintenance inhaled corticosteroid	12 (24.4)
As-needed inhaled corticosteroid and formoterol	7 (14.2)
Total IgE, kU/L, median (IQR)	58.3 (12.2-167.7)
Eosinophil count, cells/mm^3, median (IQR)	120 (72-210)
Pulmonary function test	
FEV1 (%), median (IQR)	94 (87-102)
FEV1/FVC (%), median (IQR)	108 (104-112)
FEF2575 (%), median (IQR)	104 (89-114)
PEF, median (IQR)	77 (68-87)
Exercise provocation test	
Decrement of FEV1 (%)	12 (8-16)

resenting 20 of the 54 patients with a positive test (20/54, 37.0%). Pollen sensitization was the most common aeroallergen sensitization, detected in 18 patients (18/79, 22.8%) (Table I).

Presenting Symptoms

Exertional dyspnea (94.9%) and exertional cough (81%) were the most commonly reported symptoms, followed by nocturnal cough (48.1%) and non-exertional cough (43%), (Table I).

Laboratory Findings

The median total IgE level was 58.3 kU/L (IQR: 12.2-167.7), and the median blood eosinophil count was 120 cells/mm^3 (IQR: 72-210). Baseline pulmonary function tests showed a median FEV1 of 94% (IQR: 87-102%), FEV1/FVC (FVC: forced vital capacity) ratio of 108% (IQR: 104-112%), and FEF25-75 of 104% (IQR: 89-114%) (Table I).

Treatment

Among the 51 patients diagnosed with asthma, 32 (32/51, 62.7%) were receiving maintenance therapy with inhaled corticosteroids and long-acting beta-agonists (ICS/LABA), 12 (12/51, 23.5%) were on maintenance ICS alone, and 7 (7/51,13.7%) were treated with as-needed inhaled ICS/formoterol.

Pre-exercise ICS/formoterol was recommended for the 10 patients with EIBwa for use before exercise in daily life. Among the 44 patients with EIBa, those receiving regular daily ICS therapy were advised to use a short-acting beta-agonist (SABA) before exercise. Patients receiving maintenance or as-needed ICS/formoterol therapy were instructed that an additional dose of ICS/formoterol could be used prior to exercise, in accordance with current GINA guidelines (9).

DISCUSSION

In this retrospective study, we investigated exercise-induced bronchospasm among pediatric patients who underwent an exercise bronchial provocation test and explored its association with a diagnosis of asthma.

A positive exercise bronchial provocation test was identified in 68.4% of the study population. Among those with a positive test, 44 (44/54, 81.4%) patients were diagnosed with EIB associated with asthma, while 10 patients (18.6%) were diagnosed with EIB without asthma. EIB can occur in both asthmatic and non-asthmatic individuals; however, it has been shown to be more prevalent among those with asthma. Studies have reported that the prevalence of EIB ranges from 40% to 90% among children and adolescents with asthma**,** whereas it varies between 5% and 20% in the general population (10-12). In our study, 77.8% of patients diagnosed with EIB had underlying asthma. As demonstrated in our findings, although EIB is more commonly observed in asthmatic individuals, evaluating EIB in non-asthmatic individuals presenting with exercise-related respiratory symptoms remains crucial. Recognition of EIBwa is clinically important, as these patients may benefit from pre-exercise prophylaxis with ICS/formoterol (2,13,14). NPV of 72% indicates that a negative test result

does not reliably exclude asthma, underscoring the need for clinical correlation in diagnostic decision-making.

Interestingly, despite a negative exercise provocation test, seven children were subsequently diagnosed with asthma based on clinical features and response to asthma treatment. This highlights the possibility of negative exercise challenge tests and underscores the need for a comprehensive clinical assessment when evaluating suspected asthma (14,15). Exercise bronchial provocation testing may yield false-negative results due to suboptimal exercise stimulus and day-to-day variability in airway responsiveness, particularly in milder cases. In addition, factors such as exercise intensity and duration, environmental conditions, and recent use of bronchodilator or anti-inflammatory medications may attenuate the bronchoconstrictive response during testing (1). Similar findings have been reported by Parsons and Mastronarde, who emphasized the limited sensitivity of exercise testing alone in diagnosing asthma, particularly in mild or intermittent cases (16).

In addition to asthma, allergic rhinitis and sensitization to aeroallergens have been implicated as significant risk factors for the development of EIB (17,18). Sensitization to common aeroallergens such as pollen, house dust mites, and animal dander has been shown to increase the likelihood of EIB by enhancing airway inflammation and hyperresponsiveness during exercise (19).

Moreover, studies have indicated that polysensitization may further amplify the risk of EIB compared to monosensitization, potentially reflecting a higher atopic burden and greater degree of airway inflammation (20). In our study, 37.0% of patients with EIB exhibited sensitization to at least one aeroallergen, which is consistent with prior reports linking atopy with increased bronchial hyperresponsiveness and EIB prevalence (21).

Among patients with exercise-induced bronchoconstriction, allergic rhinitis was present in 33.3% (18/54), whereas it was observed in 12% (3/25) of those with a negative exercise bronchial provocation test. Allergic rhinitis was therefore more frequent in the EIB group, underscoring the shared pathophysiological mechanisms between upper and lower airway diseases. Clinical guidelines recommend evaluating and managing coexisting allergic rhinitis in individuals with EIB, as effective treatment of nasal inflammation may mitigate symptoms during exercise (19,22,23).

In our study, 62.7 % of asthmatic patients were treated with the inhaled corticosteroids and long-acting beta-agonists combination, 23.5% with ICS monotherapy, and 13.7% with as-needed ICS/formoterol. Among patients with asthma, those receiving regular daily ICS were advised to use a SABA before exercise, whereas patients treated with maintenance or as-needed ICS/formoterol were instructed to use an additional dose of ICS/formoterol prior to exercise. These treatment strategies are consistent with both the current literature and clinical guidelines (1,3,9). Additionally, warm-up exercises prior to exertion have been shown to reduce the severity of EIB and are recommended as a non-pharmacological adjunct (24,25). Our findings underscore the importance of individualized management in pediatric patients with EIB, balancing pharmacologic treatment and supportive strategies such as pre-exercise warm-up to optimize symptom control. Furthermore, counseling on environmental precautions—such as avoiding exercise in cold, dry air, using masks or scarves to warm inhaled air, and minimizing exposure to airborne pollutants and allergens—plays a crucial role in mitigating symptom severity. Integrating these non-pharmacological measures with appropriate pharmacological management has been shown to improve disease control and enhance exercise performance (1,3).

Limitations such as its retrospective design, single-center setting, and the absence of additional bronchial provocation tests (e.g., methacholine challenge) in patients with negative exercise tests should be acknowledged. In addition, exercise bronchial provocation testing may be challenging in pediatric patients because of limited cooperation, which may influence test reliability and sensitivity (26).

The major strengths of our study include its relatively large sample size and the fact that it was conducted in a tertiary referral center with established expertise in pediatric allergy and pulmonology. Exercise bronchial provocation testing is rarely performed in children due to technical challenges and limited availability; therefore, our study represents one of the larger pediatric cohorts systematically evaluated for exercise-induced bronchoconstriction. The inclusion of detailed clinical and laboratory parameters, together with standardized testing procedures, further enhances the reliability and generalizability of our findings. Overall, this study provides valuable insights into the prevalence and clinical characteristics of exercise-induced bronchoconstriction in children, underscoring

its strong association with asthma and atopy. However, it should be noted that exercise challenge testing is not definitively diagnostic; rather, it primarily reflects exercise-induced bronchial hyperresponsiveness.

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Conflict of Interest

The authors have no conflicts of interest to declare.

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Author Contributions

Concept: **Emine Dibek Misirlioglu,** Design: **Zeynep Sengul Emeksiz,** Data collection or processing: **Funda Aytekin Guvenir, Gokhan Yorusun,** Analysis or Interpretation: **Funda Aytekin Guvenir, Gokhan Yorusun, Ahmet Selmanoglu,** Literature search: **Funda Aytekin Guvenir, Zeynep Sengul Emeksiz,** Writing: **Funda Aytekin Guvenir,** Approval: **Emine Dibek Misirlioglu.**

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