Exercise-induced bronchoconstriction in rhinitis children without asthma

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Summary

Background: **Exercise-induced bronchoconstriction (EIB) is a condition that leads to limited participation in sports. Prevalence of EIB ranges from 5-20% in general population to 40 - 90% in asthmatic patients. But the prevalence among rhinitis children with EIB remains debatable. We aimed to determine the prevalence of EIB in non-asthmatic children with rhinitis.**

Methods: **A cross-sectional study was performed on 53 rhinitis patients without known asthma who attended the Pediatric Allergy Clinic between March 2009 and February 2010.They all underwent physical examination, skin prick test, pulmonary function tests and an exercise challenge test (ECT) on a treadmill. A positive ECT was defined as a decrease in FEV_1 > 10% after exercise.**

Results: **The patients' mean age was 12.3±2.6 years. Most of them (60.4%) had moderate to severe persistent rhinitis. Eleven out of 53 patients (20.7%) had EIB. The peak time for occurrence of EIB was 10 minutes after exercise. Most of the EIB episodes observed were of mild degree. Patients who had persistent symptoms and a short duration of rhinitis treatment prior to the ECT day had more positive ECT results (72.7% vs. 28.6%, *p* 0.013, 0.2 years vs.1.9 years, *p* 0.012, respectively). The history (Hx) was not a reliable means of identifying children who had EIB (ECT+/Hx+ 54.6%, ECT-/Hx+ 54.8%). There was no significant relationship between baseline pulmonary function and the decline in FEV_1 after exercise.**

Conclusion: **The prevalence of EIB in rhinitis children without asthma is 20.7%. History, physical examination and pulmonary function are insufficient to diagnose EIB. *(Asian Pac J Allergy Immunol 2011;29:278-83)***

Key words: *rhinitis; exercise; bronchoconstriction; prevalence; exercise test*

Introduction

Exercise-induced bronchoconstriction (EIB) is the term used to describe the transient narrowing of the airways that follows vigorous exercise, with or without a history of asthma.[1] The clinical features of EIB are cough, wheezing, chest tightness and unusual shortness of breath or excess mucus occurring after a burst of strenuous and continuous aerobic exercise.[2-4] EIB is usually preceded by at least 3 to 8 minutes of exercise. Symptoms start soon after the end of exercise, peak at approximately 8 to 15 minutes and spontaneously recover within 60 minutes after the exercise ends.[5-7] Although most exacerbations are self-limited or subside readily with medication, sudden fatal asthma exacerbations can occur.[8]

The prevalence of EIB varies between 5-20% in the general population and 50 – 90% in known asthmatics.[4,9,10] Among rhinitis children the prevalence of EIB is controversial.[9, 11-13] Asthma and rhinitis often coexist and share common risk factors, including atopy, and might even be manifestations of the same disease. Several studies indicate that rhinitis can precede the onset of asthma.[14-17] Even in the pediatric population who have EIB, 30% of these patients may develop adult asthma emphasizing the importance of recognizing EIB early in life, especially in the population at risk.[18] Early recognition and intervention for EIB are essential. The aim of this study was first to determine the prevalence of EIB in non-asthmatic children with rhinitis and then to primarily identify the factors associated with EIB.

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Table 1. Baseline characteristics of patients

Characteristics	n (%)
Total number	53
Sex: Male	38 (71.7)
Female	15 (28.3)
Age (year), mean ± SD	12.3 ± 2.6
Body weight (kg), mean ± SD	46.5 ± 15.6
Height (cm), mean ± SD	149.7 ± 15.7
BMI, mean ± SD	20.3 ± 3.8
Aeroallergen sensitization (SPT+)	42 (79.3)
Diagnosed/Having history of;	
Atopic dermatitis	16 (30.2)
Allergic conjunctivitis	35 (66)
Food allergy	9 (17)
History of sinusitis	20 (37.7)
Snoring	32 (60.4)
Parental allergic rhinitis	24 (45.3)
Parental asthma	3 (5.7)
Sibling allergic rhinitis	20 (37.7)
Pet owner	27 (50.9)
Passive smoker	13 (24.5)
Breast feeding	17 (32.1)
Rhinitis data	
Age of onset (year), median (range)	5.6 (1-15)
Severity of rhinitis, n (%)	
Mild intermittent	2 (3.8)
Mild persistent	7 (13.2)
Moderate/severe intermittent	12 (22.6)
Moderate/severe persistent	32 (60.4)
Duration of treatment before ECT (year), median (range)	1.3 (0-10)
Persistent rhinitis at ECT day, n (%)	33 (62.3)
Exercise data	
Frequency of exercise (day), median (range)	3 (0-7)
Duration of exercise (minute), median (range)	45 (0-270)
History of symptoms associated with exercise, n (%)	29 (54.7)
Cough	20 (37.7)
Chest tightness	21 (39.6)
Wheezing	8 (15.1)

ECT, exercise challenge test; BMI, body mass index; SPT, skin prick test

Methods

Population

Fifty-three rhinitis children aged 7 to 18 years, attending Pediatric Allergy Clinic, Ramathibodi Hospital between March 2009 and February 2010, were asked to participate in this study. Children fulfilling the following criteria were invited: diagnosis of rhinitis according to history and physical examination, no history of asthma symptoms and normal pulmonary function [forced expiratory volume in one second (FEV_1) >80%]. Children who could not cooperate with the exercise test were excluded from the study. Informed consent was obtained from the parents of all children. This study has been approved by the Institutional Ethic Committee Board of Ramathibodi Hospital, Faculty of Medicine, Mahidol University.

Questionnaire

Parents and children were asked about the presence of atopic symptoms (asthma, allergic rhinitis, allergic conjunctivitis, atopic dermatitis) in the children. Allergic rhinitis symptoms included itching, sneezing, runny nose or blocked nose that were not associated with a cold. Grading of the severity of rhinitis was classified based on the ARIA guideline. [19] EIB was identified by asking whether the child coughs, had chest tightness, or had more breathlessness during or after exercise. Parents were asked about a history of atopic disease in parents or siblings and about environmental factors that might be associated with atopy (eg. household pets, parental smoking).

Skin prick test

Patients underwent skin prick test (SPT) with commercial extracts for Bermuda grass, Careless weed, Cladosporium, *Alternaria alternata*, *Aspergillus fumigatus*, American cockroach, German cockroach, Cat pelt, Dog pelt, Mite, *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*. The results were evaluated after 15 minutes. The test was considered positive if it elicited a wheal at least 3 mm greater in diameter than negative control.

Exercise challenge test

The exercise challenge test (ECT) was carried out using a standard protocol based on the American Thoracic Society guideline.[20, 21] Patients withheld their rhinitis medications for the appropriate time before the challenge. Caffeine and beverages or food containing caffeine were not taken before the study. Subjects did not indulge in vigorous exercise for at least 4 hours prior to attendance at the laboratory. None of the subjects had suffered from clinically apparent upper respiratory tract infections in the previous 2 weeks. All children had a physical examination before testing. Patients underwent ECT for 6-8 minutes on a treadmill achieve 80% of their maximum heart rate (220-age) or 40% of their predicted maximum voluntary ventilation (35× FEV_1). Spirometric measurements were carried out before running and repeated 5, 10, 15, 30 minutes after the end of exercise. FVC, FEV_1, maximum mid expiratory flow (MMEF) were measured in triplicate before the challenge and in duplicate after the challenge at each of the time points. All patients could perform reproducible spirometry. A positive exercise test was defined as a maximum percentage fall in $FEV_1 \geq 10\%$ from the baseline. This study

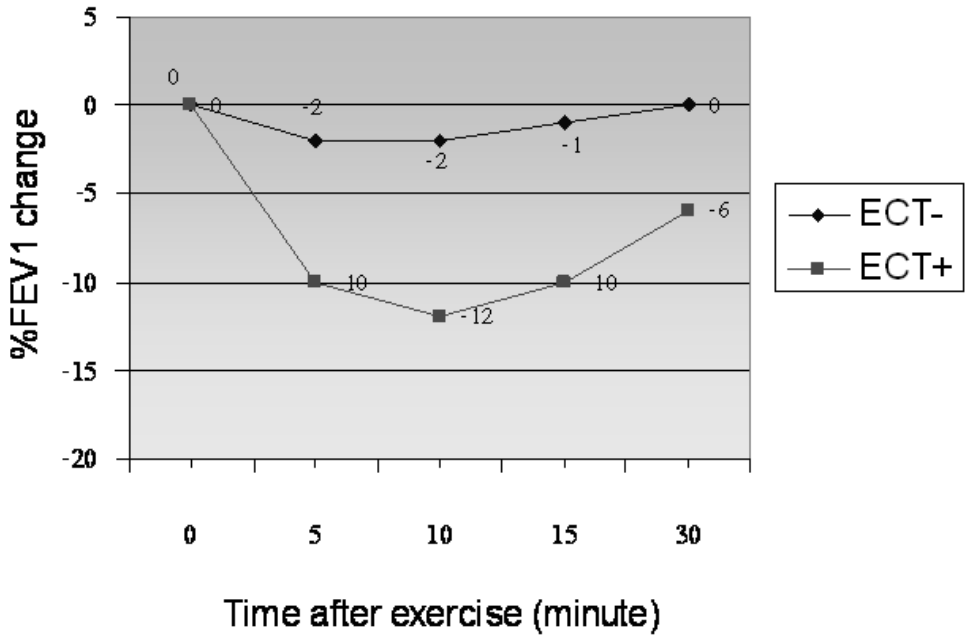

Figure 1. Pattern of FEV_1 change after the exercise test for the positive and negative exercise challenge test (ECT) groups

took place in an air-conditioned room in the same temperature conditions (25 ± 0.7 ºC) and humidity (58.6 ± 3.4 %), at a similar time of the day.

Statistical analysis

We expected the prevalence of EIB in rhinitis children at around 20% with a confidence interval of ±5%. The type one error was set at 5% and the estimated sample size was 61. However, at the conclusion of the study, because of time limitations , only 53 patients had been enrolled. The results were expressed as mean± SD or median and range. The student's *t*-test and Fisher's exact test were employed to compare the characteristics of patients with and without EIB. The level of significance was set at p <0.05. All statistics were analyzed using a statistical computer program, STATA version 11.

Results

There were 53 rhinitis children, with a mean age of 12.3±2.6 years; 71.7% were boys and 51% had a positive parental history of atopy. The median age of onset for rhinitis was 5.6 years. The majority of patients had moderate/severe persistent rhinitis (60.4%), follow by moderate/severe intermittent (22.6%), mild persistent (13.2%) and mild intermittent (3.8%) respectively. Forty-two out of 53 (79.3%) had positive SPTs for common aeroallergens, 62.3% had persistent symptoms on the day the ECT was carried out. Over 50% of children reported dyspnea during or after exercise (Table 1.).

Prevalence of EIB and ECT results

Eleven out of 53 patients (20.7%) had EIB. The peak times for EIB occurred at 10 minutes and the FEV_1 returned to normal within 30 minutes after exercise (Figure 1.). Only two patients who had FEV_1 < 10% at 30 minutes received bronchodilator and their pulmonary function returned to normal. Most EIB episodes observed were of mild degree (median FEV_1 fall 12%, range 2-30%)

Comparison of characteristics between patients with and without EIB

EIB was not related to any of the base line characteristics (age, sex, weight, height, BMI), allergic conditions (atopic dermatitis, allergic conjunctivitis, food allergy, positive family history of atopic disease) or other atopic risk factors (eg. environment, pet owner, passive smoker). But, in patients with known aeroallergen sensitization, the prevalence of EIB was less than for those without known aeroallergen sensitization (54.5% vs. 85.7%, p =0.037)

With regard to the severity of rhinitis, we found that patients who had persistent symptoms prior to

Table 2. Comparison of characteristics between patients with and without exercise-induced bronchoconstriction (EIB)

Characteristics	EIB n (%)	Non EIB n (%)	P-value
Total number	11 (20.7)	42 (79.3)	
Sex			0.48
Male	9 (81.8)	29 (69)	
Female	2 (8.2)	13 (31)	
Age (year), mean ± SD	12 ± 3	12.3 ± 2.5	0.76
Body weight (kg), mean ± SD	43.4 ± 18.2	41.3 ± 14.6	0.46
Height (cm), mean ± SD	147.6 ± 20	150.2 ± 14.7	0.63
BMI, mean ± SD	19.2 ± 4.1	20.6 ± 3.7	0.29
Pet owner	7 (63.6)	20 (47.6)	0.50
Passive smoker	1 (9.1)	12 (28.6)	0.26
Breast feeding	5 (45.5)	16 (38.1)	0.30
Parental allergic rhinitis	7 (63.6)	17 (40.5)	0.19
Parental asthma	1 (9.1)	2 (4.8)	0.51
Sibling allergic rhinitis	6 (54.6)	14 (33.3)	0.30
Atopic dermatitis	4 (36.3)	12 (28.6)	0.72
Allergic conjunctivitis	9 (81.8)	26 (61.9)	0.30
Food allergy	2 (18.2)	7 (16.7)	1.00
History of sinusitis	3 (27.3)	17 (40.5)	0.50
Snoring	7 (63.6)	25 (59.5)	1.00
Aeroallergen sensitization (SPT+)	6 (54.5)	36 (85.7)*	0.04
Median age of onset (year)	5 (1-13)	6 (2-15)	0.40
Median duration of treatment (year)	0.2 (0-3.5)	1.9(0-10)*	0.01
Persistent rhinitis at ECT day	8 (72.7)	12 (28.6)*	0.01
Median frequency of exercise (day)	3 (0-7)	3 (0-7)	0.40
Median duration of exercise (minute)	30 (0-60)	60 (0-240)	0.10
History of symptoms associated with exercise	6 (54.6)	23 (54.8)	1.00
Cough	5 (45.5)	15 (35.7)	0.73
Chest tightness	5 (45.5)	16 (38.1)	0.74
Wheezing	1 (9)	7 (16.7)	1.00
Median onset of symptoms after exercise (minute)	5 (1-20)	2.5 (1-30)	0.21
Median duration of symptoms (minute)	10 (5-20)	5 (5-30)	0.10
Baseline % FEV1/FVC, mean ± SD	86.7 ± 4.6	88.2 ± 4.5	0.31
Baseline FEV1 % predicted, mean ± SD	97.3 ± 12.5	92.2 ± 10.3	0.17
Baseline MMEF% predicted, mean ± SD	94.1 ±15.3	102.1 ± 19.9	0.22

BMI, body mass index; SPT, skin prick test; ECT, exercise challenge test; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; MMEF, maximum mid expiratory flow

the ECT day had more positive ECT results (72.7% vs. 28.6%, p = 0.013) and patients with positive ECT results had received a shorter duration of rhinitis treatment than those with negative ECT (0.2 year vs.1.9 year, p =0.012). Both patients with and without EIB had similar history of dyspnea during or after exercise. Such a history was not reliable for identifying children who had a positive ECT result (ECT+/Hx+ 54.6%, ECT-/Hx+ 54.8%). There was no significant relationship between baseline pulmonary function (FEV_1%, FEV_1/FVC, MMEF) and the decline in FEV_1 after exercise (Table 2.).

Discussion

Our data show that in children with rhinitis seen in a pediatric allergy clinic, EIB affects nearly in five rhinitis children. To the best of our knowledge, this is the first data for rhinitis children in Thailand. In previous studies, the prevalence of EIB varied from 0-41% in rhinitis patients, due to variations in the definition and methods used to detect the response.[9, 11-13] In 1976, Kawabori, et al.[9] found that 41% of atopic non-asthmatic children had a positive free running exercise test. This study was conducted in a western country. The prevalence of EIB depends on the humidity and temperature of the inspired air.[22, 23] Consequently there is some evidence to suggest that EIB may be more frequently encountered among children who live in temperate climates (western countries) than those living in tropical climates (Thailand) [10]. In 2005, Valdesoiro, et al.[13] performed a retrospective study and found that 13 of 54 allergic rhinitis patients had positive exercise stress test results. However, we cannot compare our findings with the study because of the difference in study design and the criteria used for the diagnosis of EIB. In contrast to the results of previous studies and our results, Custovic, et al.[11] found that none of 17 children with allergic

rhinitis had a positive free running exercise test. The small number and different method of assessment may explain their different findings.

Like previous studies,[24,25] we found that about half of the individuals who reported EIB symptoms had normal airway function on testing and about half of those with positive ECT results reported no symptoms. Therefore self reported symptoms were not useful in making a correct diagnosis of EIB.

Asthma and rhinitis often coexist and share common risk factors, including atopy, and might even be manifestations of the same disease. Several studies indicate that rhinitis can precede the onset of asthma.[14-17] However, few studies[15,16] have addressed the effects of rhinitis severity on the prevalence of EIB in children. Persistent rhinitis and nasal congestion will also lower the air conditioning properties of upper airway in parallel with an increase in mouth breathing that may have impact on the severity of EIB.[4] We found that patients who had persistent symptoms prior to the day of the ECT and had a short duration of rhinitis treatment had more positive ECT. These findings suggest that poor control of rhinitis may have impact on the prevalence of EIB. However, further investigations are needed.

Many studies identified that both allergic rhinitis and non allergic rhinitis are risk factor for the development of asthma.[14-16, 18] EIB in asthmatics is usually related to atopy and is associated with eosinophilia, but EIB alone without known asthma is less predictably associated with atopy.[3, 23] Our results support this evidence by determining that even rhinitis children with negative SPT results had EIB and that the prevalence of EIB was greater than in those with positive SPTs.

The management of EIB in our rhinitis children includes pharmacologic and non pharmacologic treatment. They received prophylactic short acting beta agonist bronchodilators before exercise. Non pharmacologic intervention included instructions about warming up before exercise and environmental avoidance. All patients received rhinitis treatment, were followed up regularly and closely monitored for new onset asthma, as EIB is one of the first signs of asthma to appear in childhood.

In conclusion, the prevalence of EIB in rhinitis children without asthma in Ramathibodi Hospital is 20.7%. Poor rhinitis control (persistent symptoms and short period of treatment) may increase the risk of EIB. History, physical examination and pulmonary function, either in combination or singly, are insufficient to diagnosis EIB. Thus, the exercise challenge test is essential to establish an early diagnosis and to facilitate treatment of patients at risk while helping them to successfully participate in all sports.

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