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ORIGINAL ARTICLE

Prevalence and Characteristics of Exercise-Induced Bronchoconstriction in High School and College Athletes at 2,240 m Altitude

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ABSTRACT

Background: Athletes practicing strenuous physical activities may develop exercise-induced bronchoconstriction (EIB). We aimed to determine the prevalence and features of this condition in Mexico City (altitude, 2,240 m). **Methods:** In the present study, 208 high school and college athletes performed a standardized EIB test on a treadmill. **Results:** Responses to exercise had large between-subject variability in all physiological parameters (forced expiratory volume in one second [FEV_1], heart rate, blood oxygen saturation level [SpO_2], blood pressure), with nearly similar proportions of subjects in whom FEV_1 increased or decreased. According to the recommended cut-off value of 10% FEV_1 decrease, only 15 (7.2%) athletes had a positive EIB test. Weight lifters were more prone to develop EIB (three out of seven athletes; p = 0.01). Subjects with a positive EIB test already had a lower baseline forced expiratory volume in one second/forced vital capacity (FEV_1/FVC) ratio (96.4 vs. 103.2% of predicted, respectively; p = 0.047), and developed more respiratory symptoms after exercise than subjects with a negative test. There were no differences with respect to age, gender, body mass index, history of asthma or atopic diseases, smoking habit, and exposure to potential indoor allergens. **Conclusions:** The relatively low prevalence of EIB in athletes from Mexico City raises the possibility that high altitude constitutes a protective factor for EIB. In contrast, weight lifters were especially prone to develop EIB, which suggests that repetitive Valsalva maneuvers could be a novel risk factor for EIB. There was a large between-subject variability of all physiological responses to exercise. (REV INVES CLIN. 2017;69:20-7)

Key words: Spirometry. Physical endurance. Sport medicine. Asthma.

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INTRODUCTION

Exercise is one of the most common factors capable of triggering airway obstruction in patients with asthma, and it has been estimated that up to 90% of the asthmatic population develops respiratory symptoms with exercise[1]. However, exercise may also cause bronchoconstriction in otherwise healthy persons, especially those engaging in strenuous physical activity. Exercise-induced bronchoconstriction (EIB) often appears shortly after completion of the exercise and may last for 30-90 minutes until resolution[2]. The mechanism of the airway obstruction appears to be linked to an increase in minute ventilation, which demands a higher rate of heat and water vapor transference from airway walls and produces a higher degree of cooling and hyperosmolarity of the periciliary fluid[2,3] These local changes give rise to transient shrinkage of bronchial epithelial cells and, in the case of patients with asthma, inflammatory cells such as mast cells. As the exercise level increases, the exchange of heat and water vapor progressively reaches more distant airways, and when those with a < 1 mm diameter are affected, a vascular reaction takes place causing airway wall edema and more airway obstruction[2,4].

A diagnosis of EIB is suspected when respiratory symptoms are triggered by exercise, but it must be confirmed with an exercise challenge (an EIB test). This challenge is usually performed by a standardized exercise protocol on a treadmill or a cycle ergometer[5-7], and it is considered positive when a decline of 10% or more in the forced expiratory volume at the first second (FEV_1) is observed in serial spirometries during the 30-minute period following exercise.

It has been estimated that in some high endurance sports, more than 40% of athletes present EIB[8-10], with only a small percentage of these cases linked with a diagnosis of asthma. To our knowledge, in Mexico the prevalence of EIB in athletes is unknown. The National Autonomous University of Mexico (UNAM) is the largest educational institution in Mexico, and its activities include the organization of sport activities of about 300 athletes in 52 sports, most of which require a high degree of physical performance. Recently, this institution included the EIB challenge in the group of tests available for evaluation of the athletes' health and fitness. The aim of the present report was to communicate the results of the first 208 EIB tests.

METHODS

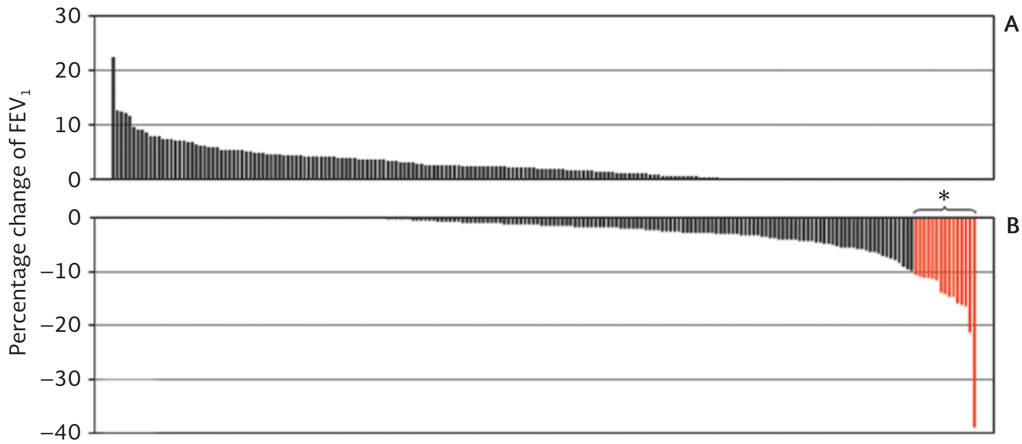
Study Population

The EIB tests were conducted at the Sport Medicine Unit facilities of the UNAM, located on the southwest of Mexico City, at an altitude of 2,240 m. Because the EIB test was part of the procedures routinely performed for the periodic clinical assessment of university athletes, approval of this retrospective study by an Institutional Review Board was unnecessary. All athletes signed a consent letter authorizing the EIB test. Exclusion criteria for an EIB test were: a self-reported heart or brain disease or any other serious illness, pregnant or lactating women, an acute upper respiratory tract infection in the last 30 days, a baseline FEV_1 < 60% of predicted or < 1.5 l, SpO_2 < 88%, or blood pressure > 180 mmHg (systolic) or > 100 mmHg (diastolic). The tests were conducted from January to August 2015, between 1 and 5 p.m. Participants were asked to wear lightweight sports clothes and have a light meal 5-6 hours prior to the EIB challenge. They should not have consumed coffee, chocolate, or cola drinks on the day of the test; should not have used bronchodilator drugs or leukotriene modifiers on the previous eight and 24 hours, respectively; and should not have engaged in vigorous exercise nor be exposed to tobacco smoke during the previous four and two hours, respectively. We completed a medical questionnaire, measured vital signs, and performed a cardiorespiratory examination. Subsequently, the EIB test was conducted as described in the following section. We recorded ambient temperature and humidity at the beginning of the EIB test, but no attempts were done to artificially control these parameters.

EIB Tests

The EIB tests were carried out according to international recommendations[5-7]. A baseline spirometry was performed with a Spirobank G® spirometer (Medical International Research, Rome, Italy) following the American Thoracic Society/European Respiratory Society guidelines[11], and results were interpreted as percentage of predicted values using the reference equations published by Hankinson, et al.[12] for Mexican-Americans. Thereafter, participants were asked to use a nose clip and to stand on the treadmill (Quinton Q65, Seattle, WA, USA), which was turned on and its velocity and inclination were progressively increased

Figure 1. Change in forced expiratory volume at first second (FEV_1) after an exercise challenge in 208 high school and college athletes. Bars represent the largest FEV_1 response of each participant, either toward bronchodilation (panel A) or toward bronchoconstriction (panel B), detected at any time point within the 30-minute post-exercise period. Athletes in panel A do not necessarily match athletes in panel B. *The exercise-induced bronchoconstriction test was considered positive when FEV_1 decreased ≥10% from baseline value.



during a 2-3 minute period until 80-90% of maximal heart rate (MHR, assessed through cardiac monitoring) or 3 miles/hour and 20° inclination were reached. MHR was calculated with the formula MHR = 220 – age in years. The exercise was maintained in these conditions for an additional four-minute period, with subsequent slow-down of velocity and decrease of the treadmill inclination until horizontality during a one-minute period. During the exercise, peripheral blood oxygen saturation (SpO_2) was measured with a pulse oximeter (Onyx® 9500, Nonin Medical Inc., Minneapolis, MN, USA), and the Borg dyspnea scale was applied at one-minute intervals. After the exercise was completed, the spirometry was repeated 5, 10, 15 and 30 minutes later. The EIB test was considered positive when any of these latter spirometries showed a 10% or more decrease in FEV_1 as compared to the baseline value. According to the degree of FEV_1 decrease, bronchoconstriction was classified as mild (≥ 10 to < 25%), moderate (≥ 25 < 50%) or severe (≥ 50%).

The majority of interval variables did not follow the normal distribution, and thus were analyzed using the Mann-Whitney *U* test. Categorical variables were analyzed with the Fisher exact test. Multivariate logistic regression (backward method) was employed to assess the capability of some variables for predicting a positive EIB test result. Likewise, predictive capability was also assessed by computing sensitivity, specificity, and positive (PPV) and negative (NPV) predictive values. Finally, Spearman correlation was used to assess the relationship between variables. Statistical significance was set at $p < 0.05$ bi-marginally.

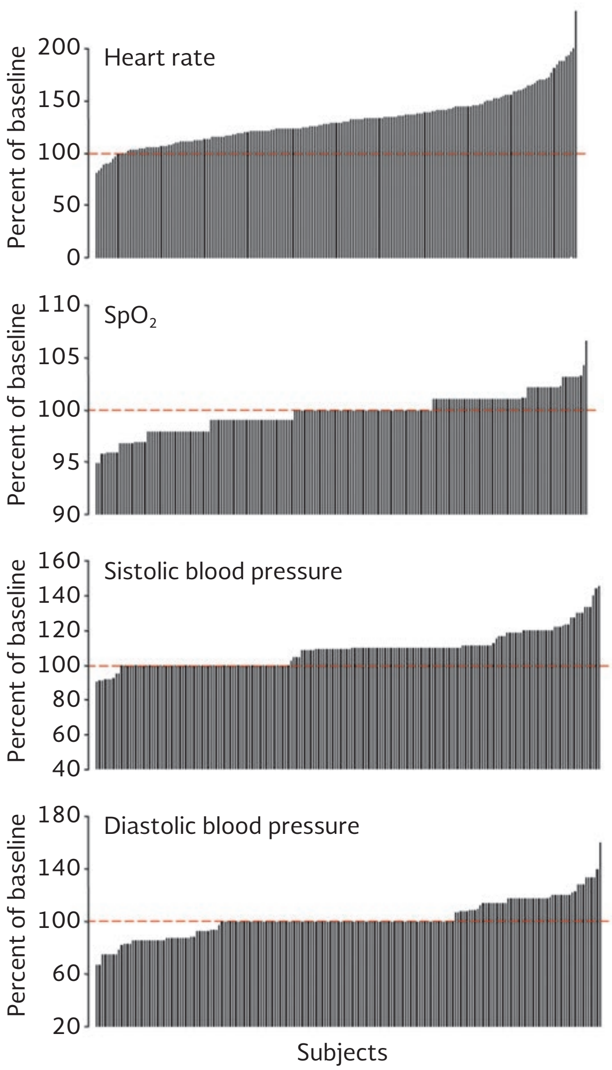
RESULTS

A population of 208 athletes from 20 summer sports, including 115 males and 93 females, with a median age of 21 years, was included in the study.

There was large between-subject variation in FEV_1 responses to the exercise challenge, with nearly equal proportions of participants in whom FEV_1 increased at any time during the 30-minute post-exercise period, and in those in whom FEV_1 decreased after exercise, as compared with their respective baseline values (Fig. 1). Other physiological parameters (heart rate, SpO_2, and systolic and diastolic blood pressures), measured five minutes after the end of the exercise also exhibited a similar pattern of highly variable responses to exercise (Fig. 2). However, changes in FEV_1 did not correlate with changes in any of these latter parameters (data not shown). Moreover, a correlation matrix revealed that post-exercise changes in these variables did not correlate with each other, except for a positive correlation between systolic and diastolic blood pressures ($r = 0.30$; $p < 0.01$) (supplemental Table S1).

According to the recommended cut-off value of a 10% decrease of FEV_1[6], 15 (7.2%) athletes had a positive

Figure 2. Changes in selected biomedical variables after an exercise challenge in high school and college athletes. Variables were measured five minutes after the end of the exercise. SpO_2: peripheral blood oxygen saturation.



EIB test, all of them developing mild airway obstruction, except for one athlete with moderate airway obstruction. Of these participants, eight reached the 10% FEV_1 decrease at five minutes after exercise, while the remaining one, two and four participants developed the airway obstruction at 10, 15 and 30 minutes after exercise, respectively.

The general characteristics of the study population, grouped as those with positive (EIB+) and negative (EIB–) tests, are depicted in table 1. There were no differences between both groups with respect to gender, age, or body mass index. The sport with the highest proportion of EIB+ athletes was weightlifting (three out of seven athletes studied, p = 0.01), followed by beach volleyball (one out of six), baseball (one out of seven), and Olympic wrestling (four out of 32). A detailed description for all sport disciplines is contained in supplemental table S2. When the sports were grouped according to their anaerobic (weightlifting, Olympic wrestling, and judo) or aerobic (the rest of the sports) requirements, the prevalence of EIB+ was higher among the former sports (17.0 vs. 4.3%, respectively; p = 0.007). However, if weight lifters were dropped from the group, the statistical significance was lost (p = 0.065, data not shown), implying that weightlifting was the main discipline accounting for the association with a positive EIB test.

Supplemental table S3 shows that athletes in the EIB+ group had a familial or personal history of asthma or atopic diseases similar to that of athletes with a negative test, with up to 6.7% and 3.6% of participants, respectively, self-reporting as being asthmatic (p = 0.46). Similarly, there were no differences between both groups regarding exposure to potential indoor allergens.

With respect to a history of exercise-related symptoms (Table 1), there was a larger proportion of participants reporting dyspnea in the EIB+ group (33.3 vs. 11.4% in the EIB– group; p = 0.03). When evaluated as a predictive factor for EIB+, dyspnea had a 33.3% sensitivity, 88.6% specificity, 18.5% PPV, and 94.4% NPV. Moreover, a multiple linear regression with exercise-related respiratory symptoms and baseline spirometry (percentage of predicted forced vital capacity [FVC], FEV_1, and FEV_1/FVC) as independent variables, demonstrated that dyspnea was the sole variable capable of predicting the amount of FEV_1 change. Up to 20% of EIB+ athletes reported the use of short-acting bronchodilators, a proportion significantly higher than that of EIB- athletes (1.6%; p = 0.006). None of the athletes who developed airway obstruction used inhaled corticosteroids. In both groups, a similarly low proportion of participants were smokers or former smokers (13% in each group, supplemental table S3).

The majority of exercise tests were performed under the environmental parameters recommended by international organizations (temperature, 20-25°C; relative humidity, ≤ 50%)[8,13] but, as a group, EIB+ athletes underwent the challenge with a slightly lower ambient temperature than the EIB– group (24 vs.

Table 1. Characteristics of 208 athletes, grouped according to results of exercise-induced bronchoconstriction test

Variable	Positive EIB test (n = 15)	Negative EIB test (n = 193)	p*
Male sex	9 (60.0)	106 (54.9)	0.79
Age (years)	21 (15-29)	21 (12-37)	0.89
Body mass index (kg/m^2)	23.9 (20.3-32.0)	23.1 (16.6-37.1)	0.63
Training (hours/week)	12 (5-36)	10 (3-30)	0.96
History of exercise-related symptoms			
Cough	2 (13.3)	19 (9.8)	0.65
Dyspnea	5 (33.3)	22 (11.4)	0.03
Wheezing	1 (6.7)	4 (2.1)	0.32
Chest tightness	1 (6.7)	13 (6.8)	1
Sputum	1 (6.7)	18 (9.4)	1
Use of short-acting beta agonists	3 (20.0)	3 (1.6)	0.006
Use of inhaled corticosteroids	0 (0)	1 (0.5)	1
Baseline spirometry (% of predicted)			
FVC	101.5 (84.5-135.0)	100.7 (71.0-137.9)	0.94
FEV_1	101.7 (78.4-126.1)	101.4 (68.9-138.5)	0.48
FEV_1/FVC	96.4 (89.8-113.7)	103.2 (88.0-118.1)	0.047
PEF	107.5 (88.9-152.6)	113.3 (81.3-157.2)	0.086
FEF_{25}	102.4 (69.2-156.1)	107.6 (55.4-156.1)	0.17
FEF_{50}	93.6 (55.7-161.6)	101.5 (47.7-187)	0.12
FEF_{75}	77.7 (53.2-170.9)	91.1 (42.7-214)	0.16

Data correspond to frequency (%) or median (minimum - maximum).
*Statistical significance evaluated with the Fisher exact test or the Mann-Whitney U test.
EIB: exercise-induced bronchoconstriction; FEF_{25}, FEF_{50}, and FEF_{75}: forced expiratory flow at 25, 50, and 75% FVC, respectively; FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; PEF: peak expiratory flow.

25°C, respectively; p = 0.03, Table 2). Only two participants, both with a negative EIB test, underwent the exercise challenge with a relative humidity of > 50%. Respiratory symptoms in the 30-minute post-challenge period were more frequently reported by EIB+ athletes, reaching statistical significance regarding dyspnea (20.0 vs. 1.2% in the EIB– group; p = 0.0042), and cough (40.0 vs. 12.7% in the EIB– group; p = 0.012). There were no differences between both groups with respect to the highest systolic or diastolic blood pressure or heart rate, but peripheral oxygen saturation was slightly lower in those with a positive EIB test (median 93 vs. 94% in the EIB– group; p = 0.041).

Before beginning the exercise challenge, athletes who eventually developed bronchoconstriction (the EIB+ group) already had lower FEV_1/FVC values than participants with a negative result, either assessed as the crude ratio (82.9% [75.4-95.2] vs. 87.1% [71.9-100], median [range]; p < 0.05) or as percentage of predicted (96.4 vs. 103.2%, respectively; p = 0.047; table 1). In addition to the 10% decrease of FEV_1, the EIB+ athletes also had an important decrease in the remaining spirometric variables after exercise, including FVC (all with a statistical significance of p < 0.001; Table 3).

DISCUSSION

In the present study, the prevalence of EIB in a group of high school and college athletes in Mexico City was 7.2%. A large multicenter study in adolescents found that the prevalence of self-reported respiratory symptoms associated with exercise varied greatly, from 6.9 to 37.5%[14]. Similarly, a number of studies in athletes have indicated that the prevalence of self-reported exercise-induced respiratory symptoms ranged from 11 to 26%, but these figures increased to more than 40% in some sports when an exercise challenge documented the EIB[8,9]. Compared with these works, the 7.2% prevalence of EIB found in our study appears to be relatively low. This discrepancy may be due to several reasons, including the type of sports evaluated, the degree of the usual exposure of athletes to urban air pollution, and the personal or familial

Table 2. Environmental conditions and clinical data during the exercise-induced bronchoconstriction test in 208 athletes

Variable	Positive EIB test (n = 15)	Negative EIB test (n = 193)	p*
Environmental conditions			
Indoor temperature (°C)	25 (23-29)	24 (15-28)	0.03
Indoor relative humidity (%)	42 (27-50)	44 (20-56)	0.47
Symptoms and signs†			
Cough	6 (40.0)	21 (12.7)	0.01
Dyspnea	3 (20.0)	2 (1.2)	0.004
Wheezing	1 (6.7)	1 (0.6)	0.16
Chest tightness	1 (6.7)	4 (2.4)	0.35
Cyanosis	1 (6.7)	0 (0)	0.08
Maximum score in the Borg scale	10 (7-16)	9 (6-19)	0.26
Physiological measurements‡			
Systolic blood pressure (mmHg)	110 (90-130)	110 (90-160)	0.98
Diastolic blood pressure (mmHg)	70 (60-90)	70 (60-110)	0.78
Heart rate (bpm)	102 (87-113)	98 (63-195)	0.29
Pulse oximetry (%)	93 (90-94)	94 (90-98)	0.04

Data correspond to frequency (%) or median (minimum-maximum).
*Statistical significance evaluated with Fisher exact test or Mann-Whitney U test.
†Detected at any point in the 30-minute period after exercise. Percentages may differ from expected because in some subjects, respiratory symptoms could not be recorded.
‡Highest value detected at any point in the 30-minute period after exercise, except for pulse oximetry, which corresponds to the lowest value.
EIB: exercise-induced bronchoconstriction.

history of atopy[8,15]. However, a further explanation of this low prevalence may be that the high altitude of Mexico City is protecting the athletes from the development of EIB. This speculation is based on the following facts. Firstly, by making a secondary analysis of published data from 154 cities included in the ISAAC study[16], it can be demonstrated that the prevalence of exercise-related wheezing among adolescents is associated with the prevalence of lifetime asthma, with a Spearman correlation coefficient of $r = 0.75$; $p < 0.001$. Secondly, the altitude strongly affects the prevalence of asthma, a condition closely related to EIB, inasmuch as asthma has a strong inverse correlation with altitude, and its frequency decreases at high altitude[16,17]. Therefore, it is possible that some of the mechanisms involved in the development of asthma also participate in the development of EIB, rendering both asthma and EIB equally sensitive to the protective effect of high altitude. In our study, the relatively low prevalence of EIB is in close agreement with the low asthma prevalence reported for Mexico City and nearby cities[17,18].

The sport with the highest prevalence of EIB was weightlifting, with up to 42.9% of participants with a positive test (three out of seven). This was surprising because EIB is usually considered to be mediated by an increase in minute ventilation[3], which obviously does not occur in weightlifting. Thus, mechanisms other than increased minute ventilation may be responsible for the EIB in weightlifting. Obesity has been implicated in higher airway hyperresponsiveness[19]. Although the use of the body mass index to evaluate obesity in athletes has some limitations[20,21], it is interesting to note that in weight lifters this index was not different from the rest of athletes (median 21.6 vs. 23.1 kg/m^2, respectively; $p = 0.59$), so obesity could be discarded as a predisposing factor. Alternatively, it is known that airway epithelium exposed to cyclical high pressure releases pro-inflammatory cytokines such as tumor necrosis factor-α (TNF-α), and interleukins IL-6 and IL-8[22,23]. Thus, it may be possible that the repetitive mechanical stress generated by the Valsalva maneuver during weight lifting could induce a certain degree of airway inflammation, leading to bronchial hyperresponsiveness to exercise. More research in a larger population of weightlifting athletes is needed in order to evaluate this last hypothesis.

Concerning gender differences, although some authors reported that female athletes tend to have a higher frequency of EIB[24], we did not observe differences in

Table 3. Spirometric changes observed after the exercise-induced bronchoconstriction test in 208 athletes

	Positive EIB test (n = 15)	Negative EIB test (n = 193)	p*
Change after exercise (% of baseline)†			
FVC	91.0 (80.1-99.2)	98.1 (85.0-110.0)	<0.001
FEV_1	85.9 (61.3-89.3)	98.7 (90.2-117.0)	<0.001
FEV_1/FVC	91.3 (76.5-100.4)	98.6 (90.3-114.0)	<0.001
PEF	78.2 (54.9-98.2)	93.8 (68.7-111.5)	<0.001
FEF_{25}	75.0 (43.4-97.7)	94.6 (71.8-113.9)	<0.001
FEF_{50}	74.9 (43.0-91.5)	95.4 (70.4-131.3)	<0.001
FEF_{75}	68.6 (46.5-102.5)	95.3 (46.4-240.7)	<0.001

Data correspond to median (minimum-maximum).
*Statistical significance evaluated with Mann-Whitney U test.
†Data correspond to the lowest measurement at any point in the 30-min period after exercise.
EIB: exercise-induced bronchoconstriction; FEF_{25}, FEF_{50}, and FEF_{75}: forced expiratory flow at 25, 50, and 75% FVC, respectively; FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; PEF: peak expiratory flow.

the male:female ratios. Likewise, it has been described that overweight and obesity are associated with EIB, and that this high airway responsiveness to exercise decreases after body weight loss[25-27]. In our study, however, the influence of body weight was negligible, inasmuch as differences in body mass index between EIB+ and EIB– groups lacked statistical significance.

Of the 208 athletes studied, eight had a medical diagnosis of asthma, yielding an overall asthma prevalence of 3.8%. This figure is in close agreement with the 4% asthma prevalence recently found among high school and college students at this same university[28]. Contrary to what may be expected, having asthma appeared not to influence the development of EIB, since only one of these athletes reached the cut-off value of a 10% decrease in the post-exercise FEV_1 value. This finding may indicate that these participants had relatively mild and well-controlled asthma. In agreement on the lack of association of asthma with EIB, other factors, such as familial or personal atopic diseases, or exposure to potential indoor allergens from pets or cockroaches, were not associated with a positive EIB test.

When we investigated a self-reported history of respiratory symptoms triggered by exercise, we found that only exercise-related dyspnea was predictive of the EIB test result. In this respect, the absence of dyspnea associated with exercise predicted a negative EIB test, with 88.6% specificity and 94.4% NPV. Conversely, the capability of a history of exercise-induced dyspnea to detect athletes who will develop EIB was poor, with 33.3% sensitivity and 18.5% PPV, as noted by others[9]. Regarding other potential predictive factors, we found that baseline spirometry did not correlate with the percentage of FEV_1 change after exercise. This finding is in contrast with the report by da Silva, et al.[26], who studied 35 adolescents with obesity and showed that a lower baseline FEV_1, but not body mass index, was predictive of a positive EIB test. The authors proposed that in this obese population, the mechanism of the EIB involves alteration of interdependent forces between airways and parenchyma that oppose airway smooth muscle contraction. Thus, differences in the type of population in our study (mainly non-obese subjects) may explain the lack of predictive capability of baseline FEV_1.

Although the main objective of an EIB test is to detect athletes with a ≥10% decrease of FEV_1, in our study it was evident that responses to the exercise challenge greatly varied among the studied participants. Compared with their respective baseline values, post-exercise FEV_1 values ranged from 122.6% (i.e., bronchodilation) up to 61.3% (i.e., bronchoconstriction). In this context, a positive EIB test may be viewed only as the edge of a wide spectrum of airway responses to exercise. The large variability in acute responses to exercise was also observed for other physiological variables, such as heart rate, SpO_2 and blood pressure. With the obvious exception of systolic and diastolic blood pressures, we did not find correlations among physiological variables, probably indicating that the mechanisms responsible for their post-exercise modifications are not the same. Exercise in general has been considered as a beneficial factor that promotes good health. However, it appears that this is not always the case. For example, Bouchard, et al.[28] analyzed the results of a study in which 1,687 persons participated in 20-26-weeks of endurance exercise programs within the context of research protocols. Changes observed in metabolic biomarkers at the end of the exercise programs exhibited wide between-subject variability, with a significant proportion of these participants developing adverse changes in fasting plasma insulin (8.4% of participants), systolic blood pressure (12.2%), plasma triglycerides (10.4%), and plasma HDL-cholesterol (13.3% of participants). Thus, the highly variable response to a long-term exercise program seemed to be replicated in the acute post-exercise changes observed in our study.

In conclusion, our study revealed that athletes practicing summer sports at a high altitude have a relatively low prevalence of EIB, defined as a post-exercise drop of ≥ 10% in FEV_1, raising the possibility that high altitude constitutes a protective factor for EIB. By contrast, weight lifters were especially prone to develop EIB, which suggests that mechanisms other than increased minute ventilation, such as repetitive Valsalva maneuvers, could also lead to EIB. Finally, we found large between-subject variability in all physiological responses to exercise.

SUPPLEMENTARY DATA

Supplementary data is available at Revista de Investigación Clínica online (www.clinicalandtranslationalinvestigation.com). These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsability of the authors.

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