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EXERCISE-INDUCED BRONCHOCONSTRICTION IN TEXTILE AND AGRICULTURAL WORKERS AND IN BAKERS

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To assess the prevalence and the characteristics of exercise-induced bronchoconstriction (EIB) in subjects occupationally exposed to organic dusts we performed a cross-sectional study including 152 exposed subjects (67 textile workers, 42 agricultural workers, and 43 bakers) and 72 unexposed controls. Evaluation of exposed and unexposed subjects included a questionnaire, skin prick tests to common inhalant allergens, spirometry, and exercise challenge tests (ECT). The EIB prevalence found in textile workers was 8.9 %, in agricultural workers 7.1 %, in bakers 6.9 %, and in office workers 5.5 %. The highest bronchial reaction to exercise was found in ECT-positive agricultural workers (26.1±6.9), followed by textile workers (25.2±7.4), bakers (23.0±5.8), and office workers (21.8±4.4). EIB was significantly associated with atopy and positive family history of asthma in all exposed groups. EIB was significantly associated with smoking duration in textile workers (P=0.039) and agricultural workers (P=0.027). Bronchial reaction to exercise was significantly greater in smoking than in non-smoking textile (P=0.045) and agricultural workers (P=0.032). Our data suggest that the combination of daily smoking and workplace exposure to certain types of organic dusts could contribute to EIB development and severity.

KEY WORDS: *dust, EIB, exercise test, exercise-induced asthma, exercise-induced bronchospasm, occupational exposure, smoking*

Exercise-induced bronchoconstriction (EIB), exercise-induced bronchospasm and exercise-induced asthma are all terms used to describe the condition of transient airflow obstruction associated with physical exertion in people who have heightened bronchial responsiveness. There is no conclusive evidence as to exact aetiology of EIB, though there are several theories. The current thinking about mechanisms by which EIB develops emphasizes the loss of heat, water or both from the airways during exercise, stemming from hyperventilation of air that is drier and cooler than that in the respiratory tree, as well as inflammatory cells present in the airways at the time of exercise (1-3).

Seventy to eighty percent of patients with current symptomatic asthma show that the exercise component to their disease and its occurrence is more frequent in patients with moderate to severely increased responsiveness (4). It is also found in about 40 % of patients with allergic rhinitis, as well as in 3 % to 11 % of non-asthmatic and non-atopic subjects (5). The diagnosis of EIB is based on a history of shortness of breath, chest tightness, cough and/or wheezing during or immediately following sustained exercise and exercise challenge test (ECT) after standardized testing protocols.

Epidemiological studies suggest increasing EIB prevalence over the last two decades, especially amongst competitive athletes. Intensive endurance training together with exposure to cold air and many inhalant irritants and allergens are thought to be causative factors (6). Although environmental and workplace air pollutants are considered as contributing factors to EIB, the effect of workplace exposure has been examined in a limited number of studies. In this study we assessed the effects of workplace exposure to different types of organic dusts on EIB development and severity.

SUBJECTS AND METHODS

Study design

A cross-sectional survey was carried out at the Department of Cardiorespiratory Functional Diagnostics, Institute of Occupational Health - WHO Collaborating Center for Occupational Health in Skopje, Macedonia from June 2004 to February 2006.

Subjects

We examined 152 subjects with workplace exposure to organic dust, including textile workers, agricultural workers, and bakers. The group of textile workers consisted of 67 subjects (26 men and 41 women, aged 28 years to 57 years) employed in spinning and packing cotton, wool, and silk fibres. Duration of employment ranged from 3 years to 26 years, mean duration (14.6$\pm$9.8) years.

Agricultural workers included 42 subjects (22 men and 20 women, aged 27 years to 54 years) employed in vegetable (tomato, pepper, cabbage, etc.) and fruit (apple, peach, apricot, etc.) cultivating. The duration of employment ranged from 4 years to 24 years, mean duration (13.1$\pm$7.2) years.

The group of bakers consisted of 43 subjects, 27 men and 16 women, aged 32 years to 54 years. The duration of employment ranged from 6 years to 23 years, mean duration (15.3$\pm$6.4) years.

In addition, a group of 72 office workers (38 men and 34 women, aged 36 years to 55 years) were included as control. Their duration of employment ranged from 4 years to 27 years, mean duration (15.7$\pm$8.1) years.

According to the classification of occupational muscular work, all exposed groups with workplace exposure to organic dust were determined to involve moderate muscular work (7).

There were no subjects in whom exercise challenge or histamine challenge were contraindicated (8, 9), nor were there subjects with the upper respiratory viral infection within three weeks before the challenge test was performed. None of the subjects took asthma medications or antihistamines at least one month before the challenge tests and skin-prick tests. Daily smokers were asked to restrain from smoking at least 3 hours before testing.

Questionnaire

The questionnaire was designed using the proposed model of the National Jewish Medical and Research Center, Denver, USA (10).

Subjects were considered having exercise-induced respiratory symptoms (EIRS) if one or more symptoms were reported: coughing during or after exercise, wheezing during or after exercise, inability to get deep breath after exercise, noisy breathing after exercise and chest tightness after exercise.

Detailed smoking history, family history of asthma and allergic diseases (taking into account the first-degree relatives), accompanying disease, and medication use were also evaluated.

Classification of smoking status was done according to the World Health Organization (WHO) guidelines on definitions of smoking status (11).

A daily smoker was defined as a subject who smoked at the time of the survey at least once a day, except on days of religious abstinence. In daily smokers we evaluated lifetime cigarette smoking ($\leq$5, 6-10, 11-20, and $\geq$21) years and daily mean of cigarettes smoked ($\leq$10, 11-20, and $\geq$21) pieces. An ex-smoker was defined as a former daily smoker who no longer smoked. Passive smoking or exposure to environmental tobacco smoke (ETS) was defined as the exposure of a person to tobacco combustion products from smoking by others (12).

Skin prick tests

Skin prick tests (SPT) to common inhalant allergens were performed in all subjects on the volar part of the forearm using commercial allergen extracts (Torlak, Serbia and Montenegro) of birch (5000 PNU), grass mixed (5000 PNU), plantain (5000 PNU), fungi mixed (4000 PNU), *Dermatophagoides pteronyssinus* (3000 PNU), dog hair (4000 PNU), cat fur (4000 PNU), and feathers mixed (4000 PNU). All tests included positive (histamine 1 mg mL^{-1}) and negative (saline 0.9 %) controls. Prick tests were considered positive if the mean wheal diameter 20 min after allergen application was at least 3 mm larger than the size of the negative control (13). Atopy was defined as the presence of at least one positive SPT (14).

Spirometry

Spirometry, including measures of forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), FEV_1/FVC ratio, and maximal expiratory flow at 50 %, 25 %, and 25 % to 75 % of FVC (MEF_{50}, MEF_{25}, and MEF_{25-75}, respectively), was performed in all subjects using spirometer Ganshorn SanoScope LF8 (Ganshorn Medizin Electronic GmbH, Germany), recording the best result from three measurements of FEV_1 that were within 5 % of each other. The results of spirometry were expressed as percentages of the predicted values according to the European Community for Coal and Steel (ECCS) norms (15).

Exercise challenge tests

The constant submaximal ECT was performed in all subjects using cycle ergometer Hellige-dynavit Meditronic 40 (Hellige GmbH, Germany). ECT was conducted in an air-conditioned room with ambient temperature of (20 to 25) °C and relative air humidity of 50 % or less. According to current recommendations, subjects exercised (8 to 10) min achieving 90 % of the predicted maximal heart rate (HR_{max}=220 - age) in the last 4 min of exercise (8, 9). Heart rate was monitored continuously throughout exercise and for five minutes after its completion from a three-lead electrocardiographic configuration. The measurements of FEV_1 were performed before and 1 min, 3 min, 5 min, 7 min, 10 min, and 15 min after exercise, and the subjects inhaled a bronchodilator (salbutamol 200 μg) upon completion of the protocol.

The response to exercise was expressed as fall index FEV_1 (100 x [preexercise FEV_1 – lowest postexercise FEV_1]/preexercise FEV_1). EIB was defined as fall index FEV_1 ≥10 % (8). Bronchial reaction after ECT in each exposed group was expressed as the mean value.

Statistical analysis

Continuous variables were expressed as means with standard deviations (SD), whereas nominal variables were expressed as numbers and percentages. The chi-square test was used for testing the difference in prevalence. Spirometric measurements and fall index FEV_1 values were compared using the independent-samples *t*-test. The chi-square test (or Fisher's exact test where appropriate) was used for testing the association between EIB and studied variables (sex, age, body mass index, baseline FEV_1, atopy, family history of asthma and allergies, daily smoking, ex-smoking, passive smoking, and duration of exposure in the exposed workers). The Mann-Whitney *U*-test was used for testing the association between EIB in daily smokers with smoking experience and daily cigarette consumption. A P-value less than 0.05 was considered statistically significant. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 11.0 for Windows.

RESULTS

Table 1 shows the characteristics of the study subjects. The prevalence of EIRS was similar in both

Table 1 *Characteristics of the study subjects*

Variable	Textile workers N=67	Agricultural workers N=42	Bakers N=43	Office workers N=72
Sex / M/W ratio	0.8	1.1	1.5	1.1
Age / years	40.2±9.7	45.9±6.5	41.7±5.9	45.8±6.1
BMI / kg/m^2	24.3±3.4	25.7±4.9	27.4±5.5	27.7±3.8
Duration of exposure / years	14.6±9.8	13.1±7.2	15.3±6.4	/
Family history of asthma	6 (8.8)	4 (9.5)	3 (6.9)	7 (9.7)
Family history of allergic diseases	6 (8.8)	5 (11.9)	4 (9.3)	6 (8.3)
Daily smokers	24 (35.8)	18 (42.8)	16 (37.2)	25 (34.7)
Smoking experience / years	19.2±6.2	21.6±7.7	17.8±8.1	17.3±5.8
Cigarettes per day	18.8±10.6	20.3±7.4	23.1±11.8	19.4±9.3
Ex-smokers	4 (5.9)	3 (7.1)	5 (11.6)	7 (9.7)
Passive smokers	10 (14.9)	7 (16.6)	7 (16.2)	11 (15.2)

Numerical data are expressed as means with standard deviations; the frequencies of positive family history of asthma and allergic diseases, daily smokers, ex-smokers, and passive smokers as the number and percentage of subjects.
M: men; W: women; BMI: body mass index.

exposed and unexposed workers with inability to get deep breath as the most frequent symptom in all exposed groups (Figure 1). The prevalence of atopy was similar in both exposed and unexposed workers with mite sensitization as the most important individual common aeroallergen in all exposed groups (Figure 2). The mean values of spirometric parameters were lower in the exposed workers than controls. Statistical significance was obtained for all measured parameters in textile workers and agricultural workers, and for small airways indices in bakers (Table 2).

EIB prevalence was similar in both exposed and unexposed workers, and the highest was in textile workers. Bronchial reaction to exercise was also similar in the exposed and unexposed workers, with agricultural workers showing the greatest reaction (Table 3).

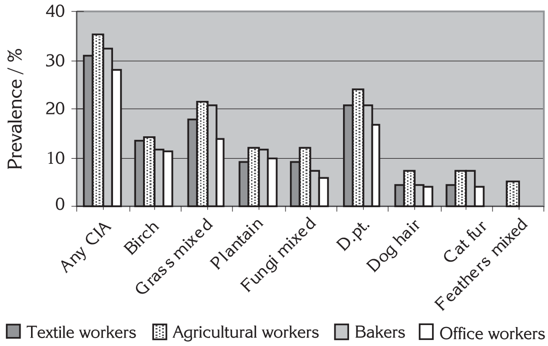

Figure 2 *Prevalence of sensitisation to CIA in textile and agricultural workers, bakers, and office workers. CIA: common inhalant allergen; D. pt.: Dermatophagoides pteronyssinus*

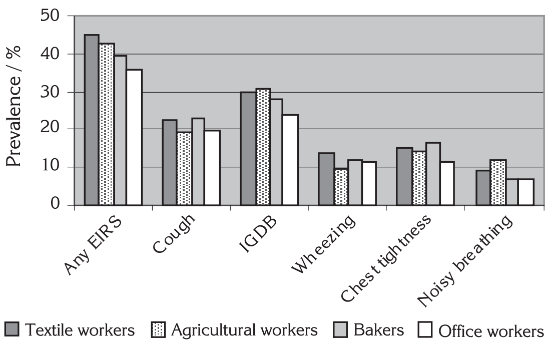

Figure 1 *Prevalence of EIRS in textile and agricultural workers, bakers, and office workers. EIRS: exercise-induced respiratory symptoms; IGDB: inability to get deep breath*

Table 4 shows mean exercise load and mean time of EIB occurrence in the ECT-positive subjects. EIB in both the exposed and unexposed workers was non-significantly associated with sex, age, BMI, baseline lung function (FEV_1 less or more than 80 % of the predicted value), and exposure duration (≤10 years and ≥11 years) in the exposed workers. The association between EIB and EIRS was also statistically non-significant in all exposed groups.

EIB was significantly associated with atopy and family history of asthma in all exposed groups.

Table 2 *Spirometric parameters in the study subjects*

Spirometric parameter	Textile workers N=67	Agricultural workers N=42	Bakers n=43	Office workers N=72
FVC / %pred	91.2±11.2	91.4±11.7	97.8±11.6	102.8±9.1
FEV_1 (%pred	85.1±7.9	86.2±9.6	91.4±9.5	97.0±9.6
FEV_1/FVC / %	73.6± 3.8	74.1±5.5	77.3±4.7	79.4±3.4
MEF_{50} / %pred	65.9±8.8	63.9±14.6	74.7±11.2	87.4±13.2
MEF_{25} / %pred	59.1±8.2	55.0±11.2	67.0±7.9	77.8±11.9
MEF_{25-75} / %pred	78.8±12.6	80.3±15.8	84.7±11.9	103.7±14.4

Data are expressed as means with standard deviations.
FVC: forced vital capacity; FEV_1: forced expiratory volume in one second; MEF_{50}, MEF_{25}, MEF_{25-75}: maximal expiratory flow at 50 %, 25 % and 25-75 % of FVC, respectively; % pred: % of predicted value.

Table 3 *EIB prevalence and intensity in the study subjects*

Occupation group	EIB prevalence / % (n)	Mean fall index FEV_1 in the subjects with positive ECT / %
Textile workers (N=67)	8.9 (6)	25.2±7.4
Agricultural workers (N=42)	7.1 (3)	26.1±6.9
Bakers (N=43)	6.9 (3)	23.0±5.8
Office workers (N=72)	5.5 (4)	21.8±4.4

EIB prevalence is expressed as the percentage and the number of subjects affected ; mean fall index FEV_1 as means with standard deviations.
EIB: exercise-induced bronchoconstriction; FEV_1: forced expiratory volume in one second; ECT: exercise challenge test.

Table 4 *Mean exercise load and mean time of EIB occurrence in the ECT-positive subjects*

Variable	Textile workers N=67	Agricultural workers N=42	Bakers N=43	Office workers N=72
Mean exercise load / W	104.1±17.9	112.4±12.8	109.3±20.4	107.7±21.3
Mean time of EIB occurrence / min after exercise	6.3±3.0	7.1±3.8	6.7±2.4	7.0±2.7

Data are expressed as means with standard deviations.
EIB: exercise-induced bronchoconstriction; ECT: exercise challenge test; N: total number

The association between EIB and family history of allergies was significant in textile workers (P=0.023; Fisher's exact test) and bakers (P=0.041; Fisher's exact test).

EIB was non-significantly associated with daily smoking in all exposed groups. Bronchial reaction to exercise in textile and agricultural workers was significantly higher in daily smokers, whereas in bakers and office workers there was no statistical difference in the bronchial reaction to exercise between smokers and non-smokers (Table 5). EIB was significantly related to smoking duration in textile workers (P=0.039; Mann-Whitney *U*-test) and agricultural workers (P=0.027; Mann-Whitney *U*-test), whereas in bakers and office workers this relationship was not statistically significant. The association between EIB and daily mean of cigarettes smoked was non-significant in all exposed groups. Ex-smoking and passive smoking were also non-significantly associated with EIB in all exposed groups.

Table 5 *Mean fall index FEV_1 in smokers and non-smokers*

Occupation group	FEV_1		P - value*
	Smokers	Nonsmokers	
Textile workers	9.4±2.8	4.3±3.1	0.045
Agricultural workers	10.1±3.9	4.2±3.8	0.032
Bakers	8.2±2.2	5.4±2.7	0.334
Office workers	6.4±2.8	5.8±3.4	0.618

Data are expressed as means with standard deviations.
FEV_1: forced expiratory volume in one second.
* Tested by independent-samples t-test.

DISCUSSION

Epidemiological studies suggest that workplace exposure to organic aerosols is frequently associated with adverse respiratory effects. On the other hand, EIB is a common condition affecting physical and occupational activities that is still underrecognized. In this study we compared EIB occurrence and characteristics between workers exposed to different types of organic dusts and working in conditions of moderate muscular demand and unexposed controls.

All exposed groups consisted of subjects with similar demographic characteristics. All had a large proportion of daily and passive smokers, similar to industrial workers from our earlier studies (16). The prevalence of ex-smokers was low. Similarly, Janson et al. (17) reported a decline in both active and passive smoking rates in 12 European countries, Australia and the USA since the early 1990s, indicating lower quitting rates and higher risk of passive smoking among people with fewer qualifications and less skilled occupation groups.

We found a high prevalence of EIRS in all exposed groups. Similar results were reported by several studies that analysed the effect of organic and mineral dust on respiratory health (18, 19). The proportion of major complaints in our study was within the range of published data (20).

The prevalence of atopy and the pattern of allergic sensitisation in both the exposed and control subjects was comparable to our earlier findings among adults in Macedonia (21, 22). Spirometric parameters were lower in the exposed workers, confirming the view that exposure to organic dust is associated with chronic airflow obstruction, predominantly affecting the smaller airways (23, 24).

The occurrence of EIB depends on the degree of airway hyperresponsiveness, exercise intensity, and ambient conditions. Many studies emphasise that cold and dry air, airborne pollutants (dust, tobacco smoke, and automobile exhaust), and allergens may trigger EIB, enhancing the airway inflammation and inflammatory mediator release (2, 3, 25). On the other hand, there were suggestions that a diet supplement with fish oil had a protective effect on EIB, which may be attributable to its anti-inflammatory properties (26). A number of studies indicated that EIB was more common in competitive athletes than in general population, and that it was more frequent in winter than in summer sport events, with prevalence varying from 12 % in basketball players to 55 % in cross-country skiers (27-29). Dust is considered a contributing factor in EIB development, but available literature there lacks data about its prevalence in workers exposed to organic and mineral dusts. We found a higher EIB prevalence in all exposed groups than in unexposed controls, but statistical difference was not established for any of them. Bronchial reaction to exercise was greater in the ECT-positive exposed workers, but there was no significant difference from positive controls. Similar results were found in our earlier study on EIB prevalence and characteristics in herbal and fruit tea processing workers (30).

We found no positive association between EIB and sex, age, body mass index, and baseline FEV_1 in any of the groups, as well as between EIB and exposure duration in the exposed workers. We also found no significant correlation between overall and particular EIRS and the results of ECT in any of the groups. Several studies confirmed that self-reported EIRS are poor predictors of actual EIB, indicating that breathing difficulties during or after exercise may be related to other conditions than bronchial obstruction, such as vocal cord dysfunction, respiratory infections, heart diseases, gastroesophageal reflux, anxiety, as well as poor physical fitness (31-34).

In our study, EIB was significantly related to positive family history of asthma in all groups. In textile workers and bakers, a significant association was also found with positive family history of allergic diseases. We found a close relationship between EIB and atopy in all exposed groups. The complex relationship between atopy and EIB is still not clear. Atopic background of airway lability is confirmed in several studies but EIB may also occur in non-atopic subjects (36-38).

The studies that investigated respiratory effects of the workplace exposure to organic dust and tobacco smoke interaction produced somewhat inconsistent results. In a Dutch contribution to ECRHS, *de Meer et al*. (39) reported non-significant interaction between workplace exposure to organic dust and smoking with respect to respiratory impairment. On the other hand, respiratory effects of the tobacco smoke in subjects with workplace exposure to different organic dusts may vary. In this study, the relationship between EIB and daily smoking, ex-smoking, and passive smoking was not significant in any of the groups. We found a significantly greater bronchial reaction after challenge in daily smoking than in non-smoking textile and agricultural workers. We also found a significant association between EIB and smoking duration in the textile and agricultural workers who were daily smokers. Similar results were found in our earlier study with herbal and fruit tea processing workers (30).

This study has some limitations. A relatively smaller number of subjects in the exposed groups could have certain implications on the data obtained and their interpretation. We were unable to perform environmental measurements in the plants of all exposed groups, so we could not document the effect of the level of exposure on EIB. At the time, we also had no standardised workplace allergen extracts for all examined groups, so we could not document sensitisation to workplace allergens and its relationship to EIB.

In conclusion, our cross-sectional study of subjects occupationally exposed to different organic dusts showed a similar EIB prevalence in the exposed and unexposed workers. Bronchial reaction to exercise was non-significantly greater in the ECT-positive, exposed workers. No significant association between the reported EIRS and the results of the exercise challenge was established for any of the groups. EIB was strongly associated with atopy and family history of asthma in all groups, as well as with family history of allergic diseases in textile workers and bakers. Bronchial reaction to exercise and EIB were significantly associated with daily smoking and smoking duration in textile and agricultural workers. Our data suggest that regular medical examination in workers exposed to organic dusts is required to detect affected individuals and institute preventive measures. More effective anti-smoking strategies are also required in order to prevent the combined effect of workplace exposure and tobacco smoke on respiratory health.

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Sažetak

BRONHOKONSTRIKCIJA UZROKOVANA TJELESNIM OPTEREĆENJEM U TEKSTILNIH I POLJOPRIVREDNIH RADNIKA I PEKARA

Svrha je ovoga ispitivanja bila utvrditi prevalenciju i značajke bronhokonstrikcije uzrokovane tjelesnim opterećenjem (EIB) u ispitanika profesionalno izloženih organskoj prašini, a obuhvatilo je 152 izložena ispitanika (67 tekstilnih radnika, 42 poljoprivredna i 43 pekara) te 72 neizložena, kontrolna ispitanika. Procjena je obuhvatila upitnik, *skin-prick* testove na uobičajene inhalacijske alergene, spirometriju te testove tjelesnim opterećenjem (ECT). Prevalencija EIB-a u tekstilnih radnika bila je 8,9 %, u poljoprivrednih radnika 7,1 %, u pekara 6,9 %, a u uredskih radnika 5,5 %. Najčešće su bronhalnu reakciju iskazali ECT-pozitivni poljoprivredni radnici (26,1±6,9) %, zatim tekstilni radnici (25,2±7,4) %, pekari (23,0±5,8) % i na kraju uredski radnici (21,8±4,4) %, ali razlike nisu bile statistički značajne. EIB je značajno povezan s atopijom i obiteljskom povijesti astme u svim izloženim skupinama radnika. Usto je EIB bio značajno povezan s trajanjem pušenja u tekstilnih (P=0,039) i poljoprivrednih radnika (P=0,027). Bronhalna reakcija na opterećenje bila je značajno veća u tekstilnih (P=0.045) i poljoprivrednih radnika (P=0.032) pušača u odnosu na nepušače. Naši podaci upućuju na to da svakodnevno pušenje može u kombinaciji s profesionalnom izloženosti određenim vrstama organskih prašina pridonijeti nastanku i stupnju bronhokonstrikcije uzrokovane tjelesnim opterećenjem.

KLJUČNE RIJEČI: *astma uzrokovana opterećenjem, bronhospazam uzrokovan opterećenjem, EIB, prašina, profesionalna izloženost, pušenje, test tjelesnog opterećenja*

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