Exercise-induced bronchoconstriction in female cleaners: effect of smoking

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Background. *Airborne particles and pollutants, such as dust, tobacco smoke and automobile exhaust, are considered as stimulants that contribute to the development of exercise-induced bronchoconstriction (EIB).* ***Objective.*** *To evaluate prevalence of EIB and its relation to smoking in female cleaners.* ***Methods.*** *We performed a cross-sectional study including 43 female cleaners aged 26 to 57 (mean age 36.9±7.6), with duration of exposure 5 to 24 years (mean duration 11.6±5.5). In addition, 45 female office workers (aged 27 to 58, mean age 38.1±5.7) were studied as a control. Evaluation of exposed and unexposed workers included completion of a questionnaire, skin prick tests to common aeroallergens, spirometry, and constant submaximal exercise challenge test (ECT) on cycle ergometer.* ***Results.*** *We found similar EIB prevalence in both cleaners and office workers (9.3% vs. 6.7%; P=0.276). Bronchial reaction to exercise, expressed as a mean fall index FEV1, was significantly greater in ECT positive cleaners (23.4% vs. 16.1%, P=0.041). EIB was strongly linked to atopy and positive family history for asthma in both groups. EIB was non-significantly associated with daily smoking in office workers (P=0.276), whereas in cleaners that association just missed significance (P=0.074). Association between EIB and daily mean of cigarettes consumed was significant in smoking cleaners (P=0.039), whereas its association with smoking experience was non-significant in both groups. Bronchial reaction to exercise was significantly greater in exposed than in unexposed smokers (9.4% vs. 4.5%; P=0.036). Association of EIB with ex- and passive smoking was non-significant in both occupation groups. Conclusions. Our data suggest that daily smoking could interact with workplace exposure in development and severity of EIB in female cleaners.*

Key words: *exercise-induced bronchoconstriction, exercise test, female, occupational exposure, smoking.*

Exercise-induced bronchoconstriction (EIB), also referred to as exercise-induced bronchospasm and exercise-induced asthma (EIA), is a manifestation of bronchial hyperresponsiveness (BHR) that occurs in the majority of patients with current symptomatic asthma[1]. Controversy remains about the causative mechanism in the bronchoconstrictive response to exercise. The most plausible current theory emphasizes airway dehidratation and hyperosmolarity that lead to mast cell degranulation and release of mediators (histamine, leukotrienes, and prostaglandins)[2, 3]. Airborne particles and pollutants, such as dust, tobacco smoke, automobile exhaust pollutants, as well as airborne allergens, are considered as stimulants that contribute to EIB[4].

Results from several studies indicated that BHR prevalence is higher in females than in males[5, 6, 7, 8]. In some of them, sex difference was explained by difference in airway geometry between females and males, while other studies suggested that the prevalence of BHR remained higher in females, even after adjustment of airway caliber[5, 6, 7]. Other mechanisms potentially responsible for a higher susceptibility of the airways in females to nonspecific stimuli include body height (males are taller than females during the adulthood), greater cholinergic irritability, hormonal factors, etc[8].

In addition, despite the controversial results of the studies on effect of smoking on respiratory impairment, there are suggestions that smoking females had an increased risk of BHR than smoking males[9].

In the present study we assessed the effect of smoking on EIB development and severity in female cleaners.

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, R. Macedonia, from June 2004 to March 2006.

Subjects

An office cleaning staff, including 43 females aged 26 to 57 years with duration of employment 5 to 24 years, was studied as exposed group. The workplace exposure of this group included dust and a variety of high- and low-molecular weight sensitizers and irritants from various cleansing agents (detergents, antiseptics, disinfectants, etc). According to the European Community Respiratory Health Survey (ECRHS) classification of occupations, cleaning was classified in the occupational set „Cleaners"[10]. According to the classification of occupational muscular work, they were determined to involve moderate muscular work[11].

In addition, a group of 45 female office workers, aged 27 to 58, was studied as a control. Unexposed controls belonged to the ECRHS occupational set „Reminder professional, administrative, clerical, service". According to the classification of occupational muscular work, they were determined to involve sedentary work.

In either group there were no subjects in whom exercise challenge was contraindicated[12, 13], nor there were 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.

Questionnaire

The questionnaire was designed using the proposed model of the National Jewish Medical and Research Center, Denver, USA[14].

Subjects were considered having exercise-induced respira-

tory 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 (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[15].

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 fasting. In daily smokers lifetime cigarette smoking (≤5, 6-10, 11-20, and ≥21 years) and daily mean of cigarettes consumed ≤10, 11-20, and ≥21) were evaluated.

Ex-smoker was defined as a formerly daily smoker, no longer smokes.

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[16].

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) of birch, grass mixed, plantain, fungi mixed, *Dermatophagoides pteronyssinus*, dog hair, cat fur, and feathers mixed. All tests included positive (1 mg/mL histamine) and negative (0.9% saline) 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[17]. Atopy was defined as the presence of at least one positive SPT[18].

Spirometry

Spirometry, including measures of forced vital capacity (FVC), forced expiratory volume in one second (FEV1), FEV1/FVC ratio, and maximal expiratory flow at 50%, 25%, and 25-75% 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) with recording the best result from three measurements the values of FEV1 of which 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[19].

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 20-25° C and relative air humidity of 50% or less. According to the actual recommendations subjects exercised 8-10 min achieving 90% of predicted maximal heart rate (HR_{max}=220–age) in the last 4 min of exercise[12, 13]. Heart rate was monitored continuously throughout exercise and for 5 minutes after its completion from a three-lead electrocardiographic configuration. The measurements of FEV_1 were performed before and 1, 3, 5, 7, 10, and 15 min after exercise, with inhaled bronchodilator application upon completion of the protocol.

The response to exercise was expressed as fall index FEV_1 (100 x [preexercise $_{FEV1}$ – lowest postexercise FEV_1]/preexercise FEV_1). EIB was defined as fall index $FEV_1 \geq 10\%$[12]. Bronchial reaction after ECT in each occupation group was expressed as mean value.

Statistical analysis

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

Results

Characteristics of the subjects enrolled in the study are given in Table1.

Prevalence of EIRS, overall and individual, was similar in both examined groups (Table 2).

Prevalence of atopy was also similar in both cleaners and office workers (32.5% and 29.1%, respectively). Mite sensitization was the most important common aeroallergen in both examined groups (20.9% and 17.7%, respectively).

Variable	*Cleaners (n = 43)*	*Office workers (n = 45)*
Age (yrs)	*36.8±7.5*	*38.1±5.7*
Body mass index (kg/m²)	*24.7±3.9*	*25.7±3.8*
Duration of employment (yrs)	*14.1±6.2*	*15.9±5.3*
Duration of exposure (yrs)	*11.6±5.5*	*/*
Positive family history of asthma	*3 (6.9%)*	*4 (8.8%)*
Daily smokers	*10 (23.2%)*	*12 (26.6%)*
Smoking experience (yrs)	*11.9±4.7*	*14.3±5.8*
Cigarettes per day	*15.8±7.4*	*12.4±5.3*
Ex-smokers	*3 (6.9%)*	*5 (11.1%)*
Passive smokers	*7 (16.2%)*	*8 (17.7%)*

Numerical data are expressed as mean value with standard deviation; the frequencies of positive family history of asthma, daily, ex-, and passive smokers as number and percentage of examinees with certain variable.
Yrs: years; kg: kilogram; m: meter.

Table 1. Characteristics of the examined subjects

EIRS	*Cleaners (n = 43)*	*Office workers (n = 45)*	*P -value**
Any EIRS	*19 (44.2%)*	*17 (37.8%)*	*0.334*
Cough	*9 (20.9%)*	*8 (17.8%)*	*0.412*
Wheezing	*6 (13.9%)*	*4 (8.9%)*	*0.215*
Inability to get deep reath	*10 (23.2%)*	*8 (17.8%)*	*0.227*
Noisy breathing	*7 (16.3%)*	*7 (15.5%)*	*0.421*
Chest tightness	*6 (13.9%)*	*5 (11.1%)*	*0.387*

Data are expressed as number and percentage of examinees with certain variable.
EIRS: exercise-induced respiratory symptoms.
** Compared using the chi-square test.*

Table 2. Prevalence of EIRS examined subjects

The mean values of spirometric parameters were lower in exposed workers than in unexposed controls. Statistical significance was obtained for all measured parameters (Table 3.).

In the group of cleaners, four subjects (9.3°%) had the fall index $FEV_1 \geq 10$°%, whereas in controls, positive ECT was noted in three subjects (6.7°%). Mean exercise load and mean time of EIB occurrence were similar in either group. Mean fall index FEV_1 in ECT positive subjects was significantly higher in cleaners (Table 4).

Spirometric parameter	Cleaners (n = 43)	Office workers (n = 45)	P -value*
FVC (%pred)	87.2±14.4	104.8±10.1	0.000
FEV1 (%pred)	82.3±9.4	96.1±6.7	0.000
FEV1/FVC%	72.6±4.1	79.6±3.8	0.000
MEF50 (%pred)	63.4±10.9	82.6±12.7	0.000
MEF25 (%pred)	51.6±12.2	74.8±10.9	0.000
MEF25-75 (%pred)	70.2±11.7	91.7±13.4	0.000
Data are expressed as the mean value with standard deviation. FVC: forced vital capacity; FEV1: forced expiratory volume in one second; MEF50, MEF25, MEF25-75: maximal expiratory flow at 50%, 25% and 25-75% of FVC, respectively; % pred: % of predicted value. * Tested using the independent samples t-test.			

Table 3. Spirometric parameters in examined subjects

Variable	Cleaners (n = 43)	Office workers (n = 45)	P- value*
Mean exercise load (Watt)	96.7±15.4	98.8±17.6	0.123
Mean fall index FEV_1 in the subjects with positive EIB (%)	23.7±4.8	16.1±5.3	0.041
Mean time of EIB occurrence (minutes after exercise)	6.4±2.3	6.9±3.1	0.108
Data are expressed as the mean value with standard deviation. FEV1: forced expiratory volume in 1 second; fall index FEV1: 100 % x (preexercise FEV_1-lowest post-exercise FEV1/pre-exercise FEV1); ECT: exercise challenge test; EIB: exercise-induced bronchoconstriction. * Compared using the independent samples t-test.			

Table 4. Mean exercise load, mean fall index FEV1 and mean time of EIB occurrence in the subjects with positive ECT

In both cleaners and controls, EIB was not significantly associated with age, BMI, and baseline FEV_1. Association between EIB and duration of exposure in cleaners was also statistically non-significant. With the exception of exercise-induced wheezing in both cleaners (P=0.019; Fisher's exact test) and controls (P=0.026; Fisher's exact test), the association between EIB and exercise-induced respiratory symptoms was not statistically significant in both occupation groups.

EIB was significantly related to atopy in both cleaners (P=0.0012; Fisher's exact test) and controls (P=0.023; Fisher's exact test). Association between EIB and positive family history of asthma was also statistically significant in both cleaners (P=0.031; Fisher's exact test) and controls (P=0.037; Fisher's exact test).

EIB was non-significantly associated with daily smoking in office workers (P=0.276; Fisher's exact test), whereas in cleaners that association just missed statistical significance (P=0.074; Fisher's exact test).

Statistical significance was found between the mean fall index FEV_1 in the exposed and control smokers (Table 5).

In exposed smokers, EIB was significantly associated with daily mean of cigarettes consumed (P=0.039; Mann-Whitney U-test), whereas its association with smoking duration was non-significant. Association of EIB with daily mean of cigarettes consumed and smoking duration in control smokers was non-significant.

	Cleaners (n = 43)	Office workers (n = 45)	P-value*
All examinees	5.8±4.9	4.3±4.0	0.112
Smokers	9.4±6.3	4.5±4.2	0.036
Nonsmokers	5.1±4.1	4.2±3.9	0.314
Data are expressed as mean value with standard deviation. * Compared using the independent-sample t-test			

Table 5. Mean fall index FEV_1 in all subjects, smokers, and non-smokers in the examined groups

Passive smoking, as well as ex-smoking were not significantly associated with EIB in either group.

Discussion

Results from several studies indicated that workplace exposure in cleaners is frequently associated with adverse respiratory effects[10, 20]. On the other hand, EIB is a common condition that is often unrecognized and uncontrolled leading affected subjects to avoid general and occupational physical activities and sports. In the present study we compared effect of smoking on the EIB occurrence and characteristics between female cleaners and unexposed female controls.

Both examined groups included subjects with similar demographic characteristics. In either group there was a large proportion of daily and passive smokers that was similar to its prevalence among females in R. Macedonia documented in our previous studies[21]. The prevalence of ex-smokers in both groups was low suggesting insufficient smoking cessation activities. The situation in the developed countries seems to be somewhat different. In the study conducted in 12 European countries as well as Australia and the USA, Janson et al.[22] reported that both active and passive smoking rates have declined since the early 1990s, but indicated lower quitting rates and higher risk of passive smoking among people with fewer qualifications and less skilled occupation groups.

We found high prevalence of exercise-induced respiratory symptoms in both examined groups that is similar to the findings of several studies that investigated EIB in different subpopulations of both sexes[23, 24]. The prevalence of atopy and the pattern of allergic sensitization to common aeroallergens in both exposed and unexposed females was comparable to that we had previously observed among adults in R. Macedonia[25]. Spirometric parameters were lower in exposed workers that confirms the constrictor effect of workplace air particles and pollutants with predominantly smaller airways affecting[26, 27].

Several studies indicated that the occurence of EIB depends on degree of bronchial hyperresponsiveness (alias underlying chronic inflammation), exercise intensity and ambient conditions[2, 3, 4]. There are many studies about EIB occurence in selected groups of general population (children, school children, adolescents, recruits), as well as in recreative and elite athletes. On the contrary, there is a limited number of studies on EIB associated with specific workplace exposures. The EIB prevalence in elite athletes varies from 12% of basketball players to 55% of cross-country skiers[28, 29]. In the present study we found similar EIB prevalence in both examined groups (9.3% and 6.7%, respectively). Similar findings were obtained in our study that investigated EIB prevalence and characteristics in herbal tea processors of both sexes[30]. Bronchial reaction to exercise in ECT positive subjects was significantly greater in cleaners than in controls. In the study of EIB in herbal tea processors we found no significant difference in bronchial reaction to exercise in ECT positive subjects from both exposed and unexposed workers. This difference may be due to the pres-

ence of subjects of both sexes among herbal tea processors, as well as to the different workplace exposures.

In both groups there was no positive association between EIB and age, BMI, and baseline FEV_1 value. EIB in both groups was strongly linked to atopy and positive family history of asthma. Similarly, in the study on elite runners Helenius et al.[31] found strong association of EIB with atopy reporting seasonal variability in EIB occurence and odds ratio increasing with number of positive skin prick tests. On the other hand, in a study with school children Penny et al.[32] reported a non-significant association of positive SPT results and specific IgE levels with positive exercise tests.

The relationship between EIB and smoking still remains unclear. In some studies, daily smoking was found to be independent determinant of BHR[5, 33]. Sunyer et al.[34] found that smoking was associated with BHR only in nonatopic subjects, while Leynaert et al.[9] reported that heavy smoking females had an increased risk of moderate to mild BHR, but no such association was found in males. On the contrary, an American study, carried out on a large sample of females (74,072) with 10 years follow-up, showed that daily smokers had a lower risk of developing asthma than never- and ex-smokers[35]. In the present study there was no association between EIB and daily smoking in controls, whereas that association in cleaners just missed significance. Statistical significance was found between the mean fall index FEV_1 in the exposed and control smokers. Paoletti et al.[8] indicated that females exhibit a dose-response relationship between daily mean of cigarettes consumed and BHR, a result not observed in males. In the present study such association was found in cleaners, but not in controls.

In the present study there was no positive association of EIB with ex- and passive smoking in both examined groups. The results from the limited number of studies that investigated link between EIB and passive smoking are controversial. In a study with school children with EIB, Agudo et al.[36] reported a significant association between EIB prevalence and exposure to environmental tobacco smoke from the mother, as well as a significantly higher risk regarding the intensity, duration and cumulative exposure. On the other hand, in a study that investigated the acute effect of ETS in children with mild asthma during rest and exercise Magnussen et al.[37] reported non-significant difference in EIRS prevalence and bronchial reaction to exercise between examinees exposed to ambient air and examinees exposed to ETS.

The present study had some limitations. Relatively smaller number of the subjects in the examined groups could have certain implications on the data obtained and its interpretation. We did not perform environmental measurements, so we could not document the effect of the level of exposure on EIB. At the time we also had no standardized workplace allergen extracts for exposed group, so we could not document sensitization to workplace allergens and its relationship to EIB.

In conclusion, in the study investigating the effect of smoking on EIB in female cleaners we found similar EIB prevalence in both examined group and significantly greater bronchial reaction to exercise in the ECT positive cleaners. EIB in female cleaners was close related to daily smoking, and a dose-response relationship between EIB and daily mean of cigarettes consumed was documented. Bronchial reaction to exercise was significantly greater in exposed than in control smokers. Our study confirms the need of more effective tobacco control measures that will prevent respiratory adverse effects of the smoking and workplace exposure interaction. Additionally, we emphasis the need of regular medical examinations in order to identify affected workers and thereby institute preventive measures.

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