

Chronic obstructive pulmonary disease in never-smoking male workers exposed to grain dust

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Abstract

Introduction. Existing literature indicates that workplace exposure to grain dust is associated with adverse respiratory effects in exposed workers. **Aim of the study.** To assess prevalence and characteristics of chronic obstructive pulmonary disease (COPD) in workers exposed to grain dust. **Material and methods.** We performed a cross-sectional study including 37 never-smoking male grain workers and an equal number of male office workers matched to grain workers by age and smoking status studied as a control. Evaluation of examined subjects consisted of completion of a questionnaire, baseline spirometry, and bronchodilator reversibility testing. **Results.** We found higher prevalence of respiratory symptoms in grain workers with significant difference for cough and phlegm. Majority

of respiratory symptoms in grain workers were work-related. The mean values of all measured spirometric parameters were significantly lower in grain workers. The prevalence of COPD, diagnosed by spirometric confirming of persistent airflow limitation, was significantly higher in grain workers as compared to office workers (10.8% vs. 2.7%, $P = 0,021$). COPD in grain workers was close related to age over 45 years and duration of employment at the actual workplace over 20 years. **Conclusions.** Our findings suggest relationship between workplace exposure to grain dust and persistent airflow limitation in exposed workers.

Key words: airflow limitation, baseline spirometry, bronchodilator reversibility testing, grain workers, office workers, questionnaire, workplace exposure.

As the frequency of the mineral dust-induced pneumoconioses decreased primarily due to the control of exposure, the obstructive airway diseases, i.e. asthma and chronic obstructive pulmonary disease (COPD), became the most prevalent work-related lung diseases.

Although cigarette smoking is considered as a major factor for the COPD development and progression, minority of smokers (around 15%) develop clinically significant COPD, suggesting that genetic predisposition and other exogenous factors are required for the development of lung injury (1). According to the American Thoracic Society (ATS) Statement for the occupational burden of airway disease (asthma, COPD, and organic dust-induced asthma-like disorder), the prevalence of COPD attributable to workplace exposures is around 15% from all COPD cases (2). In addition, the population attributable fraction (PAR) for COPD attributable to work is estimated at 19% overall and 31% among never-smokers (3). There is no doubt that certain workplace exposures enhance the risk of COPD and may do so independently of or in concert with cigarette smoking. The evidence is most coherent for work that entails exposure to coal, silica, welding fume, cadmium fume, cotton dust, farming dusts, grain dust or wood dust (4).

Grain dust is the dust produced from the harvesting, drying, handling, storage or processing of barley, wheat, oats, maize or rye and includes any contaminants or additives within the dust (e.g. bacteria, endotoxins, fungal spores, insects and insect debris, pesticide residues, silica from the soil, etc.). Processes that create grain dust include: harvesting grain and transferring

grain from combines into trailers; cleaning, dressing and drying grain; moving grain about in a grain store; transferring grain in or out of grain stores or terminals; milling and mixing dry grain; feeding dry milled grain; maintenance of plant and equipment; cleaning of buildings, vehicles, plant and equipment using compressed air or by manual/mechanical sweeping; and silo cleaning. Workplace exposure to grain dust is associated with adverse health effects, such as eye and skin irritation (i.e. conjunctivitis and skin rashes), as well as respiratory effects (rhinitis, asthma, chronic bronchitis, COPD, extrinsic allergic alveolitis, and organic dust toxic syndrome) (5).

Experimental evidence demonstrates in an animal model that exposures to organic dusts (e.g. cotton dust or corn dust) containing endotoxin or lipopolysaccharide (LPS), i.e. a heat-stable toxin associated with the outer membranes of certain Gram-negative bacteria ubiquitous in the environment, over time may share some common mechanisms of COPD. In addition, findings from experimental studies also show that chronic treatment of rabbits and hamsters with intratracheal LSP instillation causes parenchymal architectural changes in the lung that are consistent with emphysema (6, 7).

In the present study we aimed at assessment of prevalence and characteristics of COPD in never-smoking male workers exposed to grain dust.

Materials and Methods

Study design and setting

A cross-sectional study was carried out at the Institute for Occupational Health of R. Macedonia, Skopje - WHO Collaborating Center for Occupational Health and GA²LEN Collaborating Center in the period November 2014 - May 2015. Prevalence of chronic respiratory symptoms, mean values of spirometric parameters, and prevalence of COPD was compared between a group of never-smoking male grain workers and a group of never-smoking male office workers.

Subjects

We examined 37 male grain workers aged 38 to 61 years with duration of employment 15 to 29 years. They worked in two work shifts lasting 8 hours and their working tasks included cleaning, dressing and drying grain (wheat, rye, oats and corn), as well as transferring grain in or out of grain stores. The process control provided keeping of the exposures at the permissible levels. The protective equipment during the working included protective clothing, gloves, glasses, and masks. All examined grain workers were never-smokers, i.e. non-smokers who have never smoked at all, or have never been daily smokers and have smoked less than 100 cigarettes in their lifetime (8, 9).

In addition, an equal group of male office workers matched to the grain workers by age and smoking status was studied as a control.

In either group there were no subjects with chronic respiratory disease diagnosed by physician (i.e. asthma, COPD, bronchiectasis, etc.), neither subject treated

with bronchodilators and/or corticosteroids. In either group also there were no subjects in whom spirometry or bronchodilator reversibility testing was contraindicated (10, 11).

Questionnaire

An interviewer-led questionnaire was completed by all study subjects. The questionnaire included questions on work history (e.g., chronological list of jobs; description of job activities at the actual workplace; type, extent and duration of exposure; and use of protective equipment), respiratory symptoms in the last 12 months and their relatedness to the workplace, family history of COPD and CB (taking into account the first-degree relatives), environmental exposure to tobacco smoke (ETS), accompanying disease, and medication use.

Respiratory symptoms in the last 12 months (cough, phlegm, dyspnea, wheezing, and chest tightness) were documented using the European Community for Coal and Steel questionnaire (ECCS-87), and the European Community Respiratory Health Survey (ECRHS) questionnaire (12, 13). The work-relatedness of the respiratory symptoms was defined as more than usual cough, phlegm, dyspnea, wheezing, and chest tightness during daily work (14).

ETS or passive smoking was defined as an exposure to tobacco combustion products from smoking by others (at home, workplace, etc.), i.e. as a presence of at least one smoker in the household and/or in the workplace (15, 16).

Baseline spirometry

The baseline spirometry, including measures of forced vital capacity (FVC), FEV₁, FEV₁/FVC, and maximal expiratory flow at 75%, 50%, 25%, and 25-75% of FVC (MEF₇₅, MEF₅₀, MEF₂₅, and MEF₂₅₋₇₅, 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 actual recommendations of European Respiratory Society (ERS) and ATS (10, 11).

Bronchodilator reversibility testing

Bronchial reversibility testing was performed according to the actual Global Initiative for Chronic Obstructive Lung Disease (GOLD) spirometry guide (10). Spirometric measurements were performed before and 20 minutes after administration of 400 µg salbutamol by metered dose inhaler through spacer. Fixed airflow narrowing characteristic for COPD was considered if post-bronchodilator FEV₁/FVC remained less than 0.70. The degree of FEV₁ reversibility was expressed as % FEV₁ reversibility ($[\text{post-bronchodilator FEV}_1 - \text{pre-bronchodilator FEV}_1] / \text{pre-bronchodilator FEV}_1 \times 100$). Significant FEV₁ improvement (a change more than 12% and more than 200 mL) in the presence

of fixed airflow limitation did not negate a diagnosis of COPD.

COPD diagnosis

The diagnosis of COPD was established according to the actual GOLD recommendations (17), i.e., COPD was considered by the presence of a post-bronchodilator FEV₁/FVC less than 0.70 suggesting persistent airflow limitation in the subjects who had dyspnea, chronic cough or sputum production, and a history of exposure to risk factors for the disease (noxious particles and gases, i.e. tobacco smoke, smoke from home cooking and heating fuels, and/or occupational dusts and chemicals).

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), and the nominal variables as numbers and percentages. Analyses of the data included testing the differences in prevalence, comparison of the means, and testing the association between COPD and studied variables. Chi-square test (or Fisher's exact test where appropriate) was used for testing difference in the prevalence. Comparison of spirometric measurements was performed by independent-samples *T*-test. Chi-square test was used for testing association between COPD and studied variables. A *P*-value less than 0.05 was considered as statistically significant.

Results

Demographic characteristics of the study subjects were similar in both examined groups (Table 1).

Table 1. Demographics of the study subjects

Variable	Grain workers (n = 37)	Office workers (n = 37)
Age (years)	46.1 ± 5.4	45.4 ± 4.9
Less than 45 years	17 (45.9%)	18 (48.6%)
More than 45 years	20 (54.1%)	19 (52.4%)
BMI (kg/m ²)	25.3 ± 1.8	26.1 ± 2.1
BMI less than 25	18 (48.6%)	17 (45.9%)
BMI more than 25	19 (52.4%)	26 (54.1%)
Duration of employment at the actual workplace (years)	19.2 ± 3.8	20.5 ± 3.4
Duration of employment less than 20 years	16 (43.2%)	19 (52.4%)
Duration of employment more than 20 years	21 (56.8%)	18 (48.6%)
Family history of COPD or CB	5 (13.5%)	4 (10.8%)
Exposure to ETS	14 (37.8%)	12 (32.4%)
Accompanying diseases		
Arterial hypertension	5 (13.5%)	7 (18.9%)
Diabetes mellitus type 2	2 (5.4%)	3 (8.1%)
Peptic ulcer	3 (8.1%)	3 (8.1%)

Numerical data are expressed as mean value with standard deviation; frequencies as number and percentage of study subjects with certain variable.

BMI: body mass index; kg: kilogram; m: meter; COPD: chronic obstructive pulmonary disease; CB: chronic bronchitis; ETS: enirmental tobacco smoke.

Prevalence of overall respiratory symptoms in the last 12 months was higher in grain workers but statistical significance was not reached. In regard to the particular chronic respiratory

symptoms, we registered significantly higher prevalence of cough and phlegm in grain workers (Table 2).

Table 2. Prevalence of respiratory symptoms in the last 12 months in the study subjects

Respiratory symptoms in the last 12 months	Grain workers (n = 37)	Office workers (n = 37)	P-value*
Overall respiratory symptoms in the last 12 months	16 (43.2%)	9 (24.3%)	0.122
Cough	13 (35.1%)	5 (13.5%)	0.042
Phlegm	5 (13.5%)	1 (2.7%)	0.014
Dyspnea	5 (13.5%)	3 (8.1%)	0.137
Wheezing	6 (16.2%)	4 (10.8%)	0.212
Chest tightness	5 (13.5%)	4 (10.8%)	0.254

Data are expressed as number and percentage of study subjects with certain variable.

*Tested by Chi-square test (or Fisher's exact test where appropriate).

The majority of respiratory symptoms in the last 12 months in the grain workers were related to their work (81.3%). The highest relatedness with workplace was reported for cough (76.9%) and phlegm (80.0%). Work relatedness of the symptoms was reported by 22.2% of the office workers with respiratory symptoms, i.e. by two office workers with cough.

The mean baseline values of all spirometric parameters were significantly lower in grain workers (Table 3).

Table 3. Mean baseline values of spirometric parameters in the study subjects

Spirometric parameter	Grain workers (n = 37)	Office workers (n = 37)	P-value*
FVC (%pred)	95.1 ± 9.1	97.3 ± 8.3	0.034
FEV ₁ (%pred)	82.1 ± 8.2	85.2 ± 10.1	0.020
FEV ₁ /FVC	0.78 ± 0.04	0.82 ± 0.05	0.019
MEF ₇₅ (%pred)	68.6 ± 9.4	74.3 ± 11.2	0.008
MEF ₅₀ (%pred)	63.1 ± 10.9	69.4 ± 11.9	0.003
MEF ₂₅ (%pred)	54.4 ± 13.2	65.7 ± 12.8	0.000
MEF ₂₅₋₇₅ (%pred)	62.1 ± 14.3	73.4 ± 15.8	0.000

Data are expressed as mean value with standard deviation.

FVC: forced vital capacity; FEV₁: forced expiratory volume in one second; MEF₇₅, MEF₅₀, MEF₂₅, MEF₂₅₋₇₅: maximal expiratory flow at 75%, 50%, 25% and 25-75% of FVC, respectively; % pred: % of predicted value.

*Compared by Independent-samples *T*-test.

The mean post-bronchodilator values of all spirometric parameters were also significantly lower in grain workers (Table 4). In addition, the mean FEV₁ reversibility (%FEV₁ reversibility) was significantly higher in grain workers (9.4% vs. 4.3%, *P* = 0.011; Independent-samples *T*-test).

Table 4. Mean post-bronchodilator values of spirometric parameters in the study subjects

Spirometric parameter	Grain workers (n = 37)	Office workers (n = 37)	<i>P</i> -value*
FVC (%pred)	95.9 ± 10.7	98.1 ± 12.4	0.038
FEV ₁ (%pred)	85.7 ± 11.8	88.9 ± 12.9	0.015
FEV ₁ /FVC	0.79 ± 0.06	0.83 ± 0.09	0.011
MEF ₇₅ (%pred)	70.6 ± 11.7	76.8 ± 8.9	0.000
MEF ₅₀ (%pred)	65.1 ± 12.9	72.8 ± 9.4	0.000
MEF ₂₅ (%pred)	57.1 ± 14.9	69.3 ± 10.8	0.000
MEF ₂₅₋₇₅ (%pred)	67.2 ± 13.8	75.8 ± 11.3	0.000

Data are expressed as mean value with standard deviation.

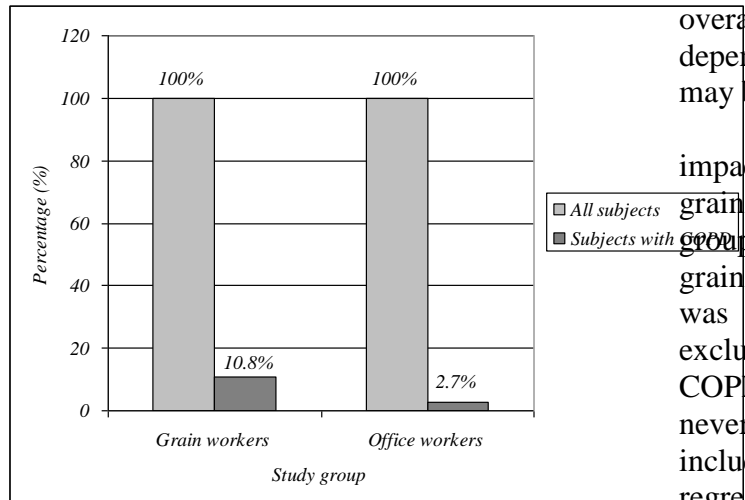
FVC: forced vital capacity; FEV₁: forced expiratory volume in one second; MEF₇₅, MEF₅₀, MEF₂₅, MEF₂₅₋₇₅: maximal expiratory flow at 75%, 50%, 25% and 25-75% of FVC, respectively; % pred.: % of predicted value.

*Compared by Independent-samples *T*-test.

Four subjects among grain workers and one subject among office workers met criteria for diagnosis of COPD (10.8% vs. 2.7%, *P* = 0,021; Fisher's exact test) (Figure 1). All grain workers with COPD reported work-relatedness of their symptoms. According to the GOLD 2010 classification

of COPD severity (18), all subjects with COPD can be categorized as a mild COPD (FEV₁/FVC < 0.70; FEV₁ ≥ 80% predicted).

Figure 1. Prevalence of COPD in the study subjects



All COPD cases in both examined groups were aged more than 45 years and were employed at the actual workplace more than 20 years. Associations between COPD and other variables (e.g., BMI, family history of COPD or CB, and environmental ETS) were statistically non-significant in both grain workers and office workers.

Discussion

COPD remains frequent and costly disease currently representing one of the principal demands of the public health worldwide. The projection of the Global Burden of Disease Study indicates that COPD in 2020 will be the third leading cause of death worldwide (from sixth in 1990) and fifth leading cause of years lost (disability-adjusted life years - DALYs) through early mortality or handicap (12th in 1990) (19). As it is mentioned earlier, according to the ATS Statement for the occupational burden of airway disease, workplace exposures are responsible for around 15% of COPD

overall but their influence is likely to vary depending on their nature and extent and may be much higher in some areas.

In the present study we assessed the impact of specific occupational exposure in grain workers on developing of COPD. A group of male office workers matched to grain workers by age and smoking status was studied as a control. As we aimed at excluding the effect of smoking on the COPD development, we examined only never-smoking workers (besides option to include smoking workers and to use regression analyses), so the examined groups included relatively small number of study subjects. The examined groups included subjects with similar demographic characteristics. In either group there was a large proportion of passive smokers (over 30%) that is similar to its prevalence among workers in R. Macedonia documented in our previous studies (20, 21) indicating insufficient nationwide smoking cessation activities.

As it is mentioned earlier, the dust to which grain workers are exposed is complex, whether it is wheat, barley, oats, corn or rye. It consists of the grain, hairs from the epicarp and the germ. Plant contaminants include weeds and pollens. Fungi grow in grain depending on its freshness. Rodents often infest it, leaving their spoor. In addition, chemicals are usually added to control fungi, insects and rodents. Free silica from the soil may be present or incorporated into the plant as phytoliths. Finally, grain workers often handle oil seeds such as sunflower, flax and mustard (22).

We found higher prevalence of respiratory symptoms in the last 12 months in grain workers than in office workers with

significantly higher prevalence of cough and phlegm. The majority of respiratory symptoms in grain workers were work-related, reaching around 80% for cough and phlegm. An excess of respiratory symptoms (either acute or chronic) were documented in several studies in grain workers, e.g. in a series of studies conducted in Canadian grain workers in the last four decades (23-27).

The mean values of all measured spirometric parameters in the present study (FVC, FEV₁, FEV₁/FVC, MEF₇₅, MEF₅₀, MEF₂₅, and MEF₂₅₋₇₅) were significantly lower in grain workers as compared to their mean values in office workers. Similar findings were reported in several cross-sectional and longitudinal studies on respiratory effects of workplace exposure to grain dust, e.g. in the studies conducted in Canadian grain workers mentioned earlier. Furthermore, in a Dutch longitudinal study with five year follow-up including around 2,000 workers in the grain processing and animal feed production, Post et al. found a significant decline in FEV₁ in the highest exposed workers compared with no and lowest exposed (28). In a study aimed at improvement of the dust control measures in the grain industry in Egypt including 200 flour mill workers, Mohammadien et al. found significantly lower mean values of FVC, FEV₁, FEV₁/FVC, MEF₇₅, MEF₅₀, and MEF₂₅ in flour mill workers than in unexposed controls with clear dose-response relationship (29).

We performed bronchodilator reversibility testing in order to detect subjects with the presence of a post-bronchodilator FEV₁/FVC less than 0.70, i.e., to confirm the diagnosis of COPD.

According to the actual GOLD recommendations, the post-bronchodilator spirometry is required for diagnosis and assessment of severity of COPD, but the degree of reversibility of airflow limitation (e.g., FEV₁ measurements before and after administration of bronchodilator) is no longer recommended. The degree of reversibility has not been shown to add to the diagnosis, differential diagnosis with asthma, or to prediction of the response to long-term treatment with bronchodilators or corticosteroids (17). We found significantly higher prevalence of COPD among grain workers than in office workers, i.e. the COPD prevalence in grain workers was fourfold higher than its prevalence in office workers. COPD in grain workers was closely related to age over 45 years and duration of employment at the actual workplace over 20 years probably reflecting the sum of cumulative exposures throughout the life in susceptible subjects. Similarly, in a South African longitudinal study with a six year follow-up including 159 milling workers, Bachmann & Myers found three-fold higher prevalence of airflow limitation (defined as FEV₁/FVC < 0.7) among the highest exposed workers compared with the lowest exposed workers (30). In addition, these findings correspond with findings from our former studies on COPD prevalence in never-smoking workers exposed to silica dust and cotton dust indicating the role of the workplace exposures to mineral and organic dust as a risk factor for COPD (31, 32).

The present study had some limitations. First, relatively small number of the subjects in the study groups could have certain implications on the data obtained and

its interpretation. Second, as in the case of any cross-sectional study, the impact of healthy workers' effect on the data obtained could not be excluded. The healthy-workers' effect (HWE) is the most common selection bias in occupational studies occurring because relatively healthy individuals are likely to gain employment and to remain employed and it may partially or completely mask excess mortality and morbidity caused by harmful exposure. Third, environmental measurements were not performed, so we could not document the effect of the type and the level of exposure on COPD. The strength of the study is the investigation of respiratory effects of the workplace exposure on never-smoking workers employed at the specific workplace within the grain industry.

Conclusions

In conclusion, in a cross-sectional study including never-smoking grain workers we found a higher prevalence of respiratory symptoms in the last 12 months, significantly higher mean values of spirometric parameters, and significantly higher prevalence of COPD than in matched office workers. COPD in grain workers was close related to age and duration of employment at the actual workplace. Our findings also indicated a need of improvement of preventive measures, i.e. proper engineering controls, respiratory protective equipment if engineering controls are not feasible and regular periodical medical examinations, in order to protect the health of exposed workers.

Competing Interests

All authors hereby have declared that no competing interests exist.

Authors Participations

JM participated in the study design, writing the protocol, data collection, managing the analyses of the study, and writing all versions of the manuscript. JKB participated in the study design, writing the protocol, managing the analyses of the study, as well as writing all versions of the manuscript. ET participated in the managing the analyses of the study and in the writing all versions of the manuscript. KV performed the statistical analysis and participated in the managing of the analyses of the study. SS and DM participated in the data collection and in the managing of the analyses of the study. All authors read and approved the final manuscript.

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