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Original Article

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Occupational factors affecting the decline in pulmonary function among male farmers using occupational pesticide in Gyeonggi-do, South Korea

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Abbreviations
CI: confidence interval; COPD: chronic obstructive pulmonary disease; FEV1: forced expiratory volume in one second; GOLD:

ABSTRACT

Background: Occupational pesticide exposure is a potential risk for respiratory health effects. Most clinical studies on pesticide exposure were related to acute exposure, and only a few studies on chronic exposure have been conducted. This study investigated the chronic respiratory health status and the chronic effects of occupational pesticide exposures of farmers in Gyeonggi-do.
Methods: Surveys and pulmonary function tests were conducted on 1,697 farmers in 16 regions of Gyeonggi-do. The structured questionnaire included demographic characteristics, medical history, recent respiratory symptoms and diseases, and work-related conditions, and was conducted through one-on-one interviews. The prevalence of respiratory diseases was compared by the odds ratios (ORs) at 95% confidence intervals (CIs) estimated by logistic regression analysis. Additional multivariate logistic regression analysis was also conducted.
Results: Pesticide work groups showed significant association with an obstructive pattern in the lung function test (unadjusted OR, 2.38; 95% CI, 1.17–5.52). Selected work-related variables of pesticide exposure were 'start age,' 'cumulative duration,' 'mixing pesticides,' and 'protection(goggle).' The obstructive pattern of lung function test showed significant associations with mixing pesticides (OR, 2.30; 95% CI,1.07–5.46), and protection (goggle) use (OR, 0.34; 95% CI, 0.12–0.79).
Conclusions: Mixing two or more pesticides showed a significant association. Wearing goggles can be seen as an indicator of awareness of the protective equipment and proper wearing of protective equipment, and loss of pulmonary function can be prevented when appropriate protection is worn.

Keywords: Pesticide; Occupational exposure; Farmers; Agriculture; South Korea; Pulmonary function test

BACKGROUND

Pesticide can be defined as "any chemical substance intended to prevent, destroy, mitigate or eliminate pests and pests, including insects, animals, weeds, and microorganisms that harm crops."[1] The types of pesticides are herbicide, insecticide, fungicide, etc. according

Global Initiative for chronic Obstructive Lung Disease; LLN: lower limit of normal; OR: odds ratio; PPE: personal protective equipment; VC: vital capacity.

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Competing interests

The authors declare that they have no competing interests.

Author Contributions

Conceptualization: Lee S, Lee SJ. Data curation: Lee S, Han J, Woo SH. Formal analysis: Lee S. Investigation: Lee S. Han J, Woo SH. Methodology: Lee S, Woo SH. Software: Lee S. Validation: Lee S. Writing - original draft: Lee S. Writing - review & editing: Lee SJ.

to their function, and can be divided into organophosphorus, organochlorine, carbamate, pyrethroid, and phenoxy according to the ingredients. It can be classified into powders, powders, granules, smokers, etc.[2] Exposure to pesticides can be occurred extensively including spraying to control pests at home or in public places, or through contamination of drinking water or food. Among them, occupational exposure of agricultural or forestry workers is the prime example of direct exposure to high concentrations. Occupational exposure to pesticide can occur during processing, storage, transport, and usage, as it can occur in mixers, loaders, greenhouse workers, and farmers.[3]

Pesticides are substances that are intended to have negative health effects and are potentially toxic to humans. In fact, it has been reported that there is a significant discrepancy between the animal test results and the toxicity results in humans.[2,4,5] Pesticides can have health effects on the human body through contact with skin and mucous membranes, or inhalation.[6] One of the main routes of occupational exposure will be inhalation.

Most clinical studies on pesticide exposure were related to acute cases, while only a few studies focused on chronic exposure, where exposure assessment studies were insufficient.[7-13] Chronic health effects represented by occupational exposure include the occurrence of various malignant tumors, respiratory system effects, neuropsychiatric effects, reproductive system and other effects. The International Agency for Research on Cancer classified the occupational pesticide exposure in farmers as a suspected carcinogen group 2A.[14] It has been demonstrated that about 12 types of pesticides show significant associations with lung cancer, pancreatic cancer, colorectal cancer, rectal cancer, leukemia, hematologic tumor, lymphoma, multiple myeloma, bladder cancer, prostate cancer, brain tumor, and skin cancer.[15] There was a report that the incidence of gastric cancer, gallbladder cancer, and liver cancer was high among male farmers who used pesticides in Korea.[16] Neuropsychiatric diseases are the representative health effects of exposure to pesticides. Diseases such as functional changes in neuro-behavior, depression, Parkinson's disease, multiple sclerosis, and amyotrophic axonal sclerosis have been reported.[1] In particular, it has been consistently reported that paraquat, one of the most used pesticides in Korea, has a significant relationship with Parkinson's disease. According to a multicenter case-control study conducted in Korea, the risk of Parkinson's disease was significantly increased by 1.6 times when farming was an occupation.[17] Reproductive system effects including a decrease in the number of sperm, a decrease in function, an increase in abnormal sperm, and a decrease in testosterone in men, and delayed menopause, menstrual cycle confusion, miscarriage, and congenital anomalies and defects in women have been reported.[18,19]

Among various types, pesticides such as Chlorpyrifos, paraquat, and parathion have a positive relationship with asthma symptoms by inhibiting cholinesterase. Asthma is generally low in farmers, but exposure to pesticides increases the risk of asthma, so the risk must be evaluated by considering the combined risk in handling pesticides.[2] Occupational pesticide exposure may be related to promoting a decrease in the forced expiratory volume in one second (FEV1) and a decrease in the percentage of inspiratory vital capacity (VC).[20] This was particularly the case in highly exposed groups working with pesticides without appropriate protective equipment, such as farmers in developing countries.[21,22]

The use of pesticides in Korea remained relatively constant in the 1990s, peaked at 28,212 tons in 2001, and decreased to about 19,131 tons by 2011. The population of farm households declined sharply from 14 million in the 1970s to 3 million in 2011 in comparison. In other words, the amount of pesticides used per person increased more than 20 times in 2011 compared to the 1970s. As for the types of pesticides currently used in Korea, in 2011, 34.7% were insecticides, 28.0% were fungicides, and 10.2% were other pesticides.[23]

On the other hand, it was found that the significance of the results varies according to the diagnostic criteria, such as the lower limit of normal (LLN) or the Global Initiative for chronic Obstructive Lung Disease (GOLD). The associations were not significant in the case of defining a doctor's diagnosis or taking medicine according to the self-reported questionnaire, whereas the case of following the GOLD or LLN criteria showed significant results.[22,24] This study used the results of pulmonary function test to define obstructive and restrictive patterns and evaluate its prevalence. This study aimed to evaluate which factors had significant respiratory effects, among chronic pesticide exposure and pesticide usage behaviors.

METHODS

Data collections

Surveys and respiratory function measurements were conducted on 1,697 farmers in 16 regions of Gyeonggi-do, including Yeoju-si, Hwaseong-si, and Anseong-si in 2013, 2014, and 2015 (3 years). 814 male farmers were remained except for missing values, those not engaged in agriculture works (non-agricultural workers), women, and those under 20 years.

A one-on-one interview was conducted using structured questionnaires consisting of agricultural work history, pesticide exposure, respiratory symptoms, diseases, etc. Male farmers classified into three groups according to the years of pesticide handling. The demographic characteristics are shown in **Table 1**. The average age of the workers exposed to pesticide over 20 years was about 61.5 (± 8.6) years old and the group never exposed to pesticide was about 55.7 (± 9.7) years old. In the age distribution, young farmers in 40s had relatively less exposure to pesticides, and farmers in 50s and 60s had the most exposure. The proportion of ever-smokers was also higher in farmers exposed to pesticide (70.8%, 77.5%) than in the never-exposed group (41.2%). Smoking status and drinking status was classified into "ever" and "never", and the "ever" group includes both past users and current users. There was no significant difference in the number of drinkers, BMI, and obesity.

Procedure

Structured questionnaire

A structured questionnaire that included demographic information, current agricultural work environment and history, and current respiratory symptoms within 6 months was conducted. To ensure homogeneity of the participants understanding the items and validity, the survey was conducted on a one-on-one basis.

Pulmonary function test

All participants were tested for pulmonary function by an experienced clinical pathologist or nurse who had been especially in charge of pulmonary function tests at Hanyang University Hospital. The equipment used for lung function testing was a MicroQuark, which was manufactured by COSMED in 2013. For each test, calibration was carried out and the clinical pathologist performed three trials; the value of most reliable trial was coded. It was classified according to the GOLD criteria as an "obstructive pattern" when FEV1/FVC (%) was less than 70%, and "restrictive pattern" when FEV1/FVC (%) was more than 70% and FVC (%) was less than 80%.

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Table 1. Demographic characteristics, prevalence of the PFT, and current respiratory symptoms

Variables	Never exposed to pesticide (n = 97)	Exposed to pesticide under 20 years (n = 281)	Exposed to pesticide over 20 years (n = 436)	*p*-value
Age (mean, years)	55.7 ± 9.7	54.1 ± 10.6	61.5 ± 8.6	0.000****
Age (group)				0.000****
Under 40	5 (5.2)	29 (10.3)	0 (0.0)	
40–49	19 (19.6)	61 (21.7)	27 (6.2)	
50–59	42 (43.3)	106 (37.7)	169 (38.8)	
60–69	24 (24.7)	68 (24.2)	157 (36.0)	
Over 70	7 (7.2)	17 (6.0)	83 (19.0)	
Smoking status				0.000****
Ever	40 (41.2)	199 (70.8)	338 (77.5)	
Never	57 (58.8)	82 (29.2)	98 (22.5)	
Drinking status				0.402
Ever	56 (57.7)	182 (64.8)	279 (64.7)	
Never	41 (42.3)	99 (35.2)	152 (35.3)	
BMI (kg/m^2)[a]	23.8 ± 3.1	25.1 ± 12.4	24.3 ± 3.1	0.236
Obesity	4 (4.1)	16 (5.7)	21 (4.8)	0.794
PFT result				0.029**
Normal	76 (78.4)	216 (76.9)	297 (68.1)	
Obstructive pattern	8 (8.2)	38 (13.5)	78 (17.9)	
Restrictive pattern	13 (13.4)	27 (9.6)	61 (14.0)	
Current respiratory symptoms				
Cough or sputum	1 (1.0)	6 (2.1)	15 (3.4)	0.320
Chest discomfort[b]	3 (3.1)	16 (5.7)	35 (8.0)	0.155
Wheezing	2 (2.1)	9 (3.2)	21 (4.8)	0.333
Allergic symptom[c]	17 (17.5)	41 (14.6)	59 (13.5)	0.593

Values are expressed as the mean ± standard deviation or number (%).
PFT: pulmonary function test; BMI: body mass index.
[a]χ^2 test: analysis of variance; [b]Chest discomfort includes dyspnea; [c]Allergic symptom includes sneezing, rhinorrhea, or nasal congestion.
Result of χ^2 test, ***p* < 0.05, *****p* < 0.001 (significant level).

Statistical analysis

All analyses were performed using R statistical software v.3.6.1 (The R Foundation, Vienna, Austria. https://www.R-project.org/).

First, for the study participants, the prevalence of obstructive and restrictive patterns in pulmonary function tests, current respiratory symptoms (cough or sputum, chest discomfort or dyspnea, wheezing, allergic symptoms) was analyzed. The odds ratios (ORs) with 95% confidence intervals (CIs) was estimated by logistic regression analysis and comparison was done by χ^2 tests.

The variables for the pesticide usage behavior were selected based on the information obtained from the self-reported questionnaire.[25] Through multivariate logistic regression analysis, significant work environment variables were selected, and a final adjusted logistic regression model was created.

Ethics statement

This study was approved by Hanyang University Institutional Review Board (HY-13-06-13) (HY-14-06-10). The contents of the study were explained to all researchers and participants, who all signed participation agreements.

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Table 2. The prevalence and OR of the PFT, current respiratory symptoms among adult male farmers

Variables	Exposed to pesticide over 20 years (n = 436)	Never exposed to pesticide (n = 97)	Unadjusted model		Adjusted model[a]	
			OR	95% CI	OR	95% CI
PFT results						
Obstructive pattern	78 (17.9)	8 (8.2)	2.38**	1.17–5.52	1.23	0.57–2.98
Restrictive pattern	61 (14.0)	13 (13.4)	1.18	0.64–2.32	0.91	0.46–1.87
Current respiratory symptoms						
Cough or sputum	15 (3.4)	1 (1.0)	3.19	0.64–57.86	2.06	3.82–38.24
Chest discomfort[b]	35 (8.0)	3 (3.1)	2.59	0.91–10.87	2.33	0.78–10.02
Wheezing	21 (4.8)	2 (2.1)	2.09	0.60–13.21	1.70	0.46–11.04
Allergic symptoms[c]	59 (13.5)	17 (17.5)	0.69	0.39–1.28	0.53**	0.28–1.01

Values are expressed as the mean ± standard deviation or number (%).
OR: odds ratio; PFT: pulmonary function test; CI: confidence interval.
[a]Adjusted for age, smoking status; [b]Chest discomfort includes dyspnea; [c]Allergic symptom includes sneezing, rhinorrhea, or nasal congestion.
Result of χ^2 test, $^{**}p < 0.05$ (significant level).

RESULTS

Of the 717 subjects in the pesticide exposed group, 38 (13.5%) and 78 (17.9%) showed an obstructive pattern and 27 (9.6%) and 61 (14.0%) showed restrictive pattern respectively, which was different from those of the never exposed group (8.2%, 13.4%). The prevalence of cough or sputum (3.4%), chest discomfort or dyspnea (8.0%), and wheezing (4.8%) symptoms was two or three times higher in the exposed pesticide over 20 years than that of the never-exposed groups (1.0%, 3.1%, and 2.1% respectively), but was not significant. On the other hand, the prevalence of allergic symptom (tears, rhinorrhea, or nasal congestion) was rather high in those who were not exposed to pesticides, though the difference was not significant.

Additional analysis related to occupational pesticide usage behavior variables among the group exposed pesticide over 20 years

Logistic regression analysis was conducted on the prevalence values to estimate ORs in **Table 2**. The exposed (over 20 years group) showed significant association with the obstructive pattern in the pulmonary function test (unadjusted OR, 2.38; 95% CI, 1.17–5.52) and allergic symptom (adjusted OR, 0.53; 95% CI, 0.28–1.01).

Additional analysis was conducted to find the associations between obstructive pattern of pulmonary function test and allergic symptoms, of which *p*-value was at significant level with pesticide usage behaviors. **Table 3** shows the significant variables of occupational pesticide usage behavior variables. These significant level variables—start age, cumulative duration (over 40 years), mixing pesticides, protection (wearing goggle)—were selected through multivariate logistic regression analysis. **Table 3** shows the final adjusted OR of obstructive pattern and allergic symptoms.

Obstructive pattern showed significant associations with mixing pesticides (OR, 2.30; 95% CI, 1.07–5.46), protection of goggle (OR, 0.34; 95% CI, 0.12–0.79). In allergic symptoms, start-age (OR, 0.23; 95% CI, 0.03–0.85), Protection of goggle (OR, 0.08; 95% CI, 0.00–0.36) showed significant associations.

DISCUSSION

The obstructive respiratory diseases include chronic bronchitis and chronic obstructive pulmonary disease (COPD), and the restrictive respiratory diseases include interstitial lung

Table 3. The final adjusted odds ratio of the prevalence of the obstructive pattern, and allergic symptoms

Variables	No. (%)	*p*-value	Adjusted OR[a]	95% CI	*p*-value
Obstructive pattern (n = 78)					
Start age					
Under 40 years	66 (85.7%)	0.439			
Over 40 years	11 (14.3%)		0.87	0.35–2.10	0.76
Cumulative duration					
Under 40 years	47 (60.3%)	0.014			
Over 40 years	31 (39.7%)		0.79	0.38–1.63	0.53
Mixing pesticides					
No	9 (11.7%)	0.049			
Yes	68 (88.3%)		2.30	1.07–5.46	0.04**
Protection					
Not wearing	72 (92.3%)	0.012			
Wearing goggle	6 (7.7%)		0.34	0.12–0.79	0.02**
Allergic symptoms (n = 59)					
Start age					
Under 40 years	55 (96.5%)	0.110			
Over 40 years	2 (3.5%)		0.23	0.03–0.85	0.06*
Cumulative durations					
Under 40 years	36 (61.0%)	0.158			
Over 40 years	23 (39.0%)		0.86	0.40–1.85	0.71
Mixing pesticides					
No	6 (10.3%)	0.059			
Yes	52 (89.7%)		1.95	0.83–5.35	0.15
Protection					
Not wearing	58 (98.3%)	0.001			
Wearing goggle	1 (1.7%)		0.08	0.00–0.36	0.01**

OR: odds ratio; CI: confidence interval.
[a]Adjusted OR: adjusted for age, smoking status, start age, cumulative duration, mixing pesticides, protection (goggle).
*$p < 0.1$, **$p < 0.05$ (significant level).

disease.[26] Asthma can be shown in both obstructive pattern and restrictive pattern as a result of pulmonary function test. In this study, there was no significant result in the cumulative spraying duration. However, a significantly positive association was observed in mixed use of pesticides with obstructive pattern, even after adjusting for confounding factors such as age, smoking, other variables of pesticide usage patterns. Mixing pesticides was defined as mixing two or more pesticide types. Types of pesticides include fungicides, insecticides, acaricides, nematodes, herbicides, plant growth regulators, mixed preparations, and the like. Furthermore, there are adjuvants to enhance their effectiveness. There are variable commercial products that are already mixed, but most Korean farmers use pesticides by directly mixing themselves before applying.[27-29] It is well known that respiratory diseases such as asthma, bronchitis, hypersensitivity diseases, and farmer's lung disease caused by organic dust, chemicals, and toxic gases have a positive correlation with pesticide exposure. The result shows COPD may also be quantitatively associated with pesticide.[30,31]

There is a difference in the types and amount of pesticides used between developed and developing countries. About 20 million tons of chemical pesticides are used worldwide each year, of which 24% are used in the United States and 45% are used in Europe. Developed countries such as Northwestern Europe, Japan, and the United States use three-quarters of the world's pesticides. While most of the pesticides used in developed countries are herbicides, insecticides are the most used in developing countries. In India, 76% of the pesticides used were insecticides and 10% were herbicides.[30] Only the cumulative time and the current status of pesticide mixing were investigated in this study, whereas the exact amount of use, and the past status of pesticide mixing, and its type were not investigated.

Joint effects due to mixing pesticides are thought to have complex and unpredictable toxicokinetic and toxicodynamic effects including metabolic and biological processes. [32-34] Most Korean farmers use pesticides by directly mixing and applying them.[35-38] About 90% of farmers already use their own blends of pesticides, and are indiscriminately mixed, abused, and misused. In a previous study in South Korea, 185 cabbage growers in the highlands of Gangwon-do had answered that they selected pesticides based on their own experience and were applying pesticides more than the standard amount (45.6%). In addition, since spraying pesticides requires significant effort, there is a tendency to roughly measure the concentration instead of actually measuring the precise amount.[36] In response to this, it is necessary to develop an appropriate restriction of misused pesticide, wear appropriate protective equipment, and blend formulation and amount taking the health hazards and risks into consideration.

Wearing goggles can be seen as an indicator of awareness in safety equipment and wearing appropriate protective equipment during work. The options available in the questionnaire were protective gloves, safety glasses, protective hat, protective clothing (top/bottom), protective boots, and mask (national certified for pesticide spraying), and the response rate was low except for masks.

Most farmers wear only a mask or even work without a mask. In Thailand, farmers wore masks, but most of them used masks composed of fabric material, which has no protection from inhalation of small particles such as pesticides.[22] A previous study on speed sprayers of Chungcheong-do, South Korea reported that 49.7% of the sprayers wore 3 (or less) personal protective equipment (PPE) during pesticide spraying, and 50.3% wore 4 (or more) PPE appropriately. By types of PPE, boots (69.2%), hats (66.4%), tops (65.4%), bottoms (64.0%), masks (54.7%), gloves (47.2%) and goggles (14.5%) were used when using pesticides. As seen above, the wear rate of goggles is relatively low.[39] In other field studies in Gyeonggi-do, the wear rate of goggles was the lowest among the PPEs generally used.[40] Therefore, wearing goggles can be seen as tendency to wear all other protective equipment and high awareness of protective equipment.

Those who wear goggles showed a significant negative association with the prevalence of both obstructive pattern and allergy symptom than those who did not wear goggles. It can be said that wearing appropriate protective equipment showed protective effects in decreased lung function.

Smoking is the strongest risk factor for obstructive lung diseases, which has been proven in several studies, including meta-analysis.[41-44] In this study, the proportion of the smoking population among pesticide exposed farmers (70.8%, 77.5%) was significantly higher than that of those never exposed to pesticides (41.2%). Furthermore, according to the results of additional analysis on pesticide exposed farmers, smoking had the highest positive association with obstructive pattern in pulmonary function test. Further evaluation for the simultaneous effects of both smoking and pesticide exposure should be conducted.

Allergic symptoms such as tears, runny nose, and mucosal irritation were negatively related in the group aged 40 years or older at the start of pesticide spraying compared to those under 40 years old. This is a result contrary to the classical hygiene theory. The hygiene hypothesis is a theory that suggests the cause of increasing allergic diseases is due to the modern urban environment living in too clean hygienic conditions.[45-47] Hygiene theory is still under debate, and there are papers claiming that the theory is still a fiction.[46] Unfortunately, to use this result as evidence to refute the hygiene hypothesis, there was no investigation regarding participant living environment. The reliability of the survey was low, because only the presence or absence of allergic symptoms surveyed with a questionnaire was identified. On the other hand, this result can be seen as a healthy worker effect.[48] This is because people with usual allergic symptoms tend to be excluded from work dealing with chemicals such as pesticide work after age 40.

This study has several strengths and limitations. It is meaningful that this study reflected the realistic agricultural environment by directly measuring and investigating the agricultural working environment and respiratory health status of South Korean farmers. In addition, the fact that most agricultural workers in South Korea are exposed to pesticides can have an important impact on the health and medical sector. Finally, related variables were selected as potential modulators of occupational pesticide exposure-related lung diseases. The results were estimated by adjusting confounding variables that have influence on respiratory function such as age and smoking status. This study provides a clue to future protective equipment design and improvement of the agricultural work environment.

This study has some limitations. Quantitative work measurements were not made; nor was further analysis executed. In addition, the control group population who did not work with pesticides was insufficient, and the morbidity of the results according to the period of pesticide work was not observed. It was not possible to evaluate the effects of other regions and climate by surveying only Gyeonggi-do. Further sensitivity analysis is needed for the effect of smoking on lung function. Detailed stratification of smoking, such as the amount of smoking and duration is necessary. The mask investigated was specified as the national certified mask for pesticide spraying, but other options were not specified. It was considered to be worn, even if it was occasionally, and duplicate responses were allowed. Questions about wearing PPE reflects the current level of the equipment worn, but the past wear rate could not be confirmed.

CONCLUSIONS

Among pesticide working behaviors, mixing pesticides showed a significant association with decline function in pulmonary test. Wearing goggles can be seen as an indicator of awareness of available protective equipment and proper wearing of protective equipment. It can be said that the obstructive lung disease and allergic symptoms was prevented when appropriate protective equipment was worn.

Considering that most farmers use pesticides directly, this result means that significant attention should be paid to improving the current agricultural work environment and behavior.

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