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SPIROMETRIC CHANGES IN RELATIONSHIP TO SERUM CHOLINESTRASE LEVELS FOR WORKERS IN A PESTICIDE-PROCESSING FACTORY

By

Abou Salem M.E., Abdel-Rasoul G.M., and Al-Batanony M. A.

FROM

Public Health and Community Medicine Department,

Faculty of Medicine, Menoufiya University

ABSTRACT

Background: occupational exposure to pesticides produces health disorders for exposed individuals by inhalation, skin contact, or ingestion. **Aim:** to study the spirometric changes in relationship to serum cholinestrase level among a group of workers employed in a pesticides processing factory. **Subjects and methods:** Fifty six pesticide-exposed males and 56 non-exposed male workers (as a control group) were chosen for this study. Each participant was subjected to a questionnaire including personal data; medical examination; serum cholinestrase level; and spirometric measurements (FVC%, FEV_1%, FEV_1/ FVC% & FEF_{75-85} %). **Results :** the respiratory manifestations as cough, expectoration, dyspnea, wheezes and crepitations were significantly more prevalent among pesticide-exposed workers than controls. Significant decrease in the serum cholinestrase level and in mean values of spirometric measurements for FVC%, FEV_1%, FEV_1/ FVC% & FEF_{75-85} % were found among pesticide-exposed workers than the control group. The decrease in studied spirometric mean values among pesticide-exposed workers was associated with increased length of duration of work. Also, there was a significant positive correlation between mean values of serum cholinestrase (ChE) among exposed workers and studied spirometric measurements: FEV_1% (r = 0.31, P < 0.05), FEV_1/ FVC% (r = 0.35, P< 0.05) & FEF_{75-85}% (r = 0.30, P< 0.05). **Recommendations:** spirometric measurements should be included in the pre-employment and periodic medical examinations to detect early changes and prevent any further decrements on occupational exposure to pesticides processing.

Introduction

Pesticide is the generalized term applied to chemicals that are used to control pests and most people know very little about pesticides There are four general classes of pesticides. Insecticides are used to control insects; rodenticides to control rodents; herbicides to control weeds; and fungicides to control fungi (Jones et al., 2006). Occupational exposure to pesticide produces many disorders for individual exposed to these toxic substances by inhalation, skin contact, or ingestion (Kennedy and Valentine, 1994).

Toxicity is a measure of the ability of a chemical to cause harmful effects. It depends on four aspects of the pesticide: (1) type and amount of active ingredient(s), (2) carrier or solvent ingredient(s), (3) inert ingredients, and (4) type of formulation (Jones et al., 2006). Pesticide formulation is the term applied to the mixture of active and inert ingredients and diluent that can be applied to a targeted pest for its control. The active ingredients are the chemicals that control the target pest. Inert ingredients are inactive and are used to dilute the pesticide or to make it safer, more effective, easier to measure, mix, and apply, and more convenient to handle. Exposure levels depend on the nature and formulation of the pesticide, utilization techniques, hygiene and environmental conditions (Van Hemmen, 1999).

In developed countries, legislation provides some protection against the dangers of occupational use of pesticides, where as in devloping countries, the safety problems are neglected and workers may not be legally protected against the toxic effects of pesticides at work (Nieuwenhuijsen, 1996). Inhalation of pesicide dust, vapours, mists and gases may therefore represent a significant occupational hazard with workers vulnerable to acute toxic episodes and chronic intoxication (Legaspi and Zenz, 1994). Disorders of the cardiovascular system, nervous system (Abdel-Rasoul et al., 2002) , liver (El-Sobky et al., 1994), sensory organs, and respiratory system and reduced lung function have been reported after exposure to pesticides (International Agency for Research on Cancer {IARC}, 1991).

Respiratory diseases have been placed at the top of the ten leading work-related diseases and injuries. Occupational asthma has become the most prevalent occupational lung disease in developed countries (International Labour Organization {ILO}, 1998). Organophosphates and carbamates, because of their effects on cholinesterase, produce bronchoconstriction but have no well-documented, long-term pulmonary effects in humans. Altogether, few pesticides other than those cited above are associated with the development of chronic or acute pulmonary disease (Steven and Vincent, 2000). Oxidative stress, present whenever some pesticides are inhaled, may initiate diseases such as chronic bronchitis, emphysema, fibrosis and cancer (Witsch and Last, 1996). Occupational asthma , reactive-airways dysfunction syndrome, or even a transient hypersensitivity elicited by irritation may occur (Seaton and Crompton, 2000).

Blood plasma contains a related enzyme called ChE or pseudo-ChE, which contributes to the whole blood enzymatic activity; the extent of the contribution of plasma-ChE will depend on which substrate was used and at what concentration. PseudoChE has no known physiological function, but can be inhibited selectively by some carbamates and organophosphates without causing a toxic response (Amr et al., 1984; Kamel et al., 1990; and Abd-Elroaf et al.,1997).

Few epidemiological studies have been conducted throughout the world to evaluate the short and the long-term effects on the respiratory system of occupational exposure to pesticides (Salameh et al., 2005). Mortality and morbidity studies are commonly performed, whereas respiratory effects have been less studied, due to the difficulty in evaluating respiratory exposure (do Pico, 1992) in addition to the confounding effect of workers' lifestyle as smoking, physical conditions,climate..etc (Blair and Zahm, 1999).

Aim of study

This study aimed at assessing the spirometric changes in relationship to serum cholinestrase level among a group of workers employed in a pesticides processing factory.

Subjects and Methods

A cross sectional study was carried out on workers in pesticides processing factory (formulation and packaging of organophosphates, carbamates and pyrithrins pesticides), Kafr El-Ziat City, Gharbia governorate, through the period from May to August 2006. This factory employs 534 workers included in two main departments:

1) adminstrative (247 employees), 2) maintenance and production (287 male manual workers). The work in this factory is three 8-hour shifts for six days a week.

The present study included approximately 20% (56 male manual workers:the exposed group) out of the total number of manual workers (287) in this factory chosen by systematic random sampling technique using staff registers, where every fifth employee was chosen. Besides, 56 male subjects were chosen from Menoufiya Faculty of Medicine workers (matched for age, sex and never occupationally exposed to pesticides) as a control group after exclusion of subjects suffering from chronic respiratory problems as asthma or chronic bronchitis diagnosed according to criteria of World health organization (WHO), (1999). The control group was of the same socioeconomic standard as that of the exposed one.

All participants were included in the study after explaining to them the objectives, methodology of the study and getting their oral consents. They were subjected to:

a) A questionnaire including: personal data as age, duration of employment, smoking habits, present history of respiratory complaints and socioeconomic status.

b) Medical examination: general; including weight and height and local examination for chest.

c) Spirometric measurements were made using a portable computerized spirometer (Spirolab II) designed for ambulatory spirometry measurements. The device measures actual respiratory flow in addition to predicted values according to age, sex, height, weight, and race as follows:

1) Forced vital capacity (FVC), i.e. volume in liters from peak inspiration to the end of the forced exhalation ;

2) Forced expiratory volume at 1st second (FEV1), i.e. the volume expired during the first second while performing the FVC;

3) FEV1/ FVC ratio; and

4) Forced expiratory flow at 75-85% (FEF75-85 %), which is the average expiration flow rate during the point at 75-85% of the FVC volume (Salameh et al.,2005).

Each spirometric test was repeated 3 times to allow the choice of the best values, according to the American Thoracic Society (1987) criteria (2 values of FEV1 and FVC should not differ by more than 5% or 100 ml) and all measured values were expressed as percentages from predicted ones. For exposed workers, spirometric measurements were conducted before work-shift (for assessing possible past chronic exposure effect to pesticides) and then conducted immediately after the work shift (for assessing possible acute exposure effect of pesticides).

d) Serum cholinestrase (ChE) level: colourimetric test for the "in vitro" determination of cholinestrase in serum using substrate butyryl thiocholine kits (Den Blawen et al.,1983) was done for exposed workers in the chemical laboratory unit affiliated to the same pesticide factory. While that for control group was done in biochemistry department in Menoufiya Faculty of Medicine by the same type of kits and the same laboratory techniqes (Normal values at 25o C for men of all ages =3500-8500 U/L).

Data were collected, tabulated and analysed using SPSS software version 11 for Chi-square (X2), Z test and student's t and paired t- tests and correlation coefficient at 5% level of significance.

Results

Ages of exposed group ranged from 28 to 59 years old (X±SD = 40.79 ± 4.17) and that were not significantly different than that of control ones which were 32 to 56 years old (X±SD = 41.13 ± 4.23), P > 0.05. Also, the percentage of smokers was not significantly different among exposed group than controls (37.5% & 41.07 %, respectively),(P> 0.05) (table 1).

Also, the studied respiratory clinical manifestations (cough, expectoration, dyspnea, wheezes and crepitations) were found significantly more prevalent among exposed group than among the controls (19.64 % Vs 5.37 %; 16.07 % Vs 3.57 %; 21.43 % Vs 5.37 %; 19.64 % Vs 3.57 %; & 14.28 % Vs 3.57 %, respectively) (P < 0.05) (table 2).

At the same time, there was a significant decrease in the mean values of studied spirometric measurements (FEV1%, FEV1/ FVC % & FEF75-85%) in pesticide-exposed workers (84.12 ± 9.17, 80.21 ± 9.91 & 91.09 ± 9.19, respectively) than that of control group (93 .91± 10.81, 98.13 ± 8.87 & 102.41 ±10.49, respectively) (P<0.05). This finding was associated with a significant decrease in the mean levels of serum ChE among exposed group than that for control one (3519.11 ± 111.21 & 3928.95 ± 114.08, respectively) (P<0.05) (table 3).

Moreover, there was a trend of reduction in the mean values of FVC %, FEV1%, FEV1/ FVC % & FEF75-85% in post- shift (86.79 ± 8.29, 83.63 ± 8.89, 79.01 ± 9.11, &90.42 ± 9.15, respectively) than that in pre- shift (87.28 ± 8.34, 84.12 ± 9.17, 80.21± 9.91,& 91.09 ± 9.1 9, respectively) among exposed workers (P>0.05)(table 4).

As regards the duration of work in years, mean spirometric values of FVC%, FEV1%, FEV1/ FVC%, & FEF75-85% significantly decreased in workers exposed to pesticides for 15 years or more (88.98 ±8.01, 85.12 ±7.17, 82.21±7.91 & 94.05 ± 8.1 9, respectively) than that for exposed for less than 15 years (85.06 ± 8.14, 81.23 ±7.89, 79.01±8.11& 91.42 ± 8.15, respectively) (P<0.05). While the mean levels of serum ChE among exposed workers did not change by the length of duration of work in pesticides processing factory (P>0.05) (table 5).

Consequently, there was a significant positive correlation between mean levels of serum ChE among pesticide-exposed workers and spirometric mean values: FEV1% (:r = 0.31 & P < 0.05), FEV1/ FVC% (r = 0.35 & P< 0.05), & FEF75-85% (r = 0.30 & P< 0.05) (table 6).

1) Demographic and social characteristics of studied groups.

Variables	Exposed No =56		Control No = 56		Test of significance	P-value
Age in years ($\bar{X}$± SD)	40.79 ± 4.17		41.13 ± 4.23		t- test = 0.43	> 0.05
Smoking habits						
-Ex-smoker (No &%)	5	8.93	4	7.14		
-Current smoker (No &%)	21	37.50	23	41.07	$X^2 = 0.17$	> 0.05
-Non-smoker (No &%)	30	53.57	29	51.79		

2) Clinical manifestations among studied groups.

Clinical manifestations	Exposed No = 56		Control No= 56		Z-test	P-value
	No	%	No	%		
Cough	11	19.64	3	5.37	2.85	< 0.05
Expectoration	9	16.07	2	3.57	2.12	< 0.05
Dyspnea	12	21.43	3	5.37	3.24	< 0.05
Wheezes	11	19.64	2	3.57	3.07	< 0.05
Crepitations	8	14.28	2	3.57	2.44	< 0.05

3) Mean values of Spirometric measurements and Serum ChE levels among studied groups.

Studied variables	Exposed (No = 56) $\bar{X}$ ± SD	Control (No = 56) $\bar{X}$ ± SD	t- test	P-value
FVC%	87.28 ± 8.34	88.06 ± 9.71	0.39	> 0.05
FEV1%	84.12 ± 9.17	93.91 ± 10.81	6.16	< 0.05
FEV1 / FVC%	80.21 ± 9.91	98.13 ± 8.87	14.62	< 0.05
FEF_{75-85}%	91.09 ± 9.1 9	102.41 ± 10.49	11.82	< 0.05
ChE U/L	3519.11 ± 111.21	3928.95 ± 114.08	12.45	< 0.05

4) Spirometric measurements before (pre-shift) and after work shift (post-shift) among pesticide-exposed subjects.

Spirometric measurements	Work shift		Paired t- test	P-value
	Pre- shift (No = 56) X ± SD	Post- shift (No = 56) X ± SD		
FVC%	87.28 ± 8.34	86.79 ± 8.29	0.49	> 0.05
FEV1%	84.12 ± 9.17	83.63 ± 8.89	0.16	> 0.05
FEV1 / FVC%	80.21 ± 9.91	79.01 ± 9.11	0.52	> 0.05
FEF_{75-85}%	91.09 ± 9.1 9	90.42 ± 9.15	0.06	> 0.05
ChE U/L	3519.11 ± 111.21	3488.95± 112.08	0.77	>0.05

5) Spirometric measurements and Serum cholinestrase (ChE) level among exposed group according to duration of work (in years).

Studied variables	Duration of work		t- test	P-value
	Exposed < 15 y. (No= 35) X± SD	Exposed ≥ 15 y. (No = 21)X± SD		
FVC%	88.98 ± 8.01	85.06 ± 8.14	2.49	< 0.05
FEV1%	85.12 ± 7.17	81.23 ± 7.89	3.16	< 0.05
FEV1 / FVC%	82.21 ± 7.91	79.01 ± 8.11	2.62	< 0.05
FEF_{75-85}%	94.05 ± 8.1 9	91.42 ± 8.15	2.46	< 0.05
ChE U/L	3527.84 ± 109.27	3511.78 ± 108.47	0.14	>0.05

6) Correlation between serum Cholinestrase level and spirometric measurements for pesticide-exposed workers.

Spirometric measurements	r	p
FVC%	0.19	> 0.05
FEV1%	0.31	< 0.05
FEV1 / FVC%	0.35	< 0.05
FEF_{75-85}%	0.30	< 0.05

Discussion

The current study reveald that the mean age (in years) and the prevalence of smokers did not differ significantly in either of the exposed or control groups (P>0.05) (table 1), Hence any difference in studied variables: spirometric measurements and serum ChE may be contributed to other risk factors including occupational exposure to pesticides.

Several studies have reported increased risk of respiratory problems, such as asthma and chronic bronchitis among pesticides exposed workers (Kimbell-Dunn et al.,2001). In this study, the respiratory manifestations were significantly prevalent among exposed workers: cough (19.64%), expectoration (16.07 %), dyspnea (21.43 %), wheezes (19.64 %), and crepitations (14.28 %) than control ones (5.37 %; 3.57 %; 5.37 %; 3.57 %; & 3.57 %, respectively) (table 2). This finding can be explained by the presence of direct respiratory irritation resulting from pesticides inhalation in this factory. Similar results were reported by Court et al., (2002), Salameh et al., (2003), and Neice et al., (2005) who found 15-17% of subjects exposed to pesticides had asthma symptoms (episodes of wheezing with shortness of breath), 27-30% had symptoms of chronic respiratory illness, 8- 9% had chronic cough, 11-13% had chronic phlegm, and 5-6% had chronic bronchitis.

Moreover, there may be an indirect action of prolonged exposure to pesticides resulting in bronchoconstriction due to decrease in serum ChE level in the exposed individuals (Steven and Vincent, 2000). This indirect action could explain the significantly lowered studied spirometric measurements (FEV1%, FEV1/ FVC % & FEF75-85%) in exposed pre-shift mean values (84.12 ± 9.17, 80.21 ± 9.91 & 91.09 ± 9.19, respectively) than in controls (93 .91± 10.81, 98.13 ± 8.87 & 102.41 ±10.49, respectively) (P<0.05, table 3). This result agrees with that obtained by

Viegi et al., (2000) who reported, the prevalence of airways obstruction from pesticides exposure was 13% according to the European criterion, 45% according to the American criterion, and 23% according to clinical symptoms. Also, the result is in concordance with that obtained by Salameh et al., (2005)) who stated that chronic exposure of workers to industrial pesticides seems to be associated with a decrease in respiratory function (of obstructive pattern).

On the other hand, the lower mean values of FEF75-85% gives an indication of peripheral airway obstruction. It is believed to be a more sensitive index of airway obstruction than the FEV1%, especially in the small airways that are dependent on the elastic and resistant properties of the distal airways than on the subject`s spirometer performance (Seaton and Crompton, 2000).

Moreover, there was a trend of reduction in the mean values of FVC %, FEV1%, FEV1/ FVC % & FEF75-85% in post- shift (86.79 ± 8.29, 83.63 ± 8.89, 79.01 ± 9.11, &90.42 ± 9.15) than that in pre- shift (87.28 ± 8.34, 84.12 ± 9.17, 80.21 ± 9.91,& 91.09 ± 9.1 9) among exposed workers in addition to a non significant decrease in ChE in post- shift (3488.95 ± 112.08) than that in pre- shift (3519.11 ±111.21) (P>0.05) (table 4). This denotes a temporary acute effect of occupational exposure to pesticides.

Synchronously, as the duration of exposure to pesticides (in years) increased the mean spirometric values of FVC%, FEV1%, FEV1/ FVC%, & FEF75-85% were significantly decreased in exposed workers for 15 years or more (88.98 ±8.01, 85.12 ±7.17, 82.21±7.91 & 94.05 ± 8.1 9, respectively) than those for exposed for less than 15 years (85.06 ± 8.14, 81.23 ±7.89, 79.01±8.11& 91.42 ± 8.15, respectively) (P<0.05). While the mean levels of serum ChE among exposed workers showed a non significant decrease with the increase in the duration of work in pesticides` processing factory (for < 15 years: 3527.84 ± 109.27 , ≥ 15 years: 3511.78 ± 108.47) (P>0.05) (table 5). This finding agrees with that obtained by Al-Saleh , (1994) and The Environmental Protection Agency (EPA), (2006) who do recognize that the degree of adverse effects to health in pesticides processing activities increases with the increase in the duration of exposure. Also, Donham et al., (2000) found in a similar study that, the prevalence of chronic bronchitis with more marked spirometric changes increased with the length of working activity in pesticides industry.

Consequently, there was a significant positive correlation between mean levels of serum ChE among pesticide-exposed workers and spirometric mean values: FEV1% (:r = 0.31 & P < 0.05), FEV1/ FVC% (r = 0.35 & P< 0.05), & FEF75-85% (r = 0.30 & P< 0.05) (table 6). As a further support to this correlation was the finding that organophosphate and carbamate compounds are thought to contribute to respiratory symptoms through ChE inhibition, which may promote bronchoconstriction, (Abd-Elroaf et al.,1997). Also, occupational exposure to paraquat was associated with increased wheeze among Nicaraguan banana workers and decreased lung function and reduction of ChE among South African farm workers (Castro-Gutierrez, et al.,1997).

Conclusion and Recommendations

This study showed that the respiratory manifestations as cough, expectoration, dyspnea, wheezes and crepitations were significantly prevalent among pesticide-exposed workers (due to direct irritation of respiratory tree by pesticides) than controls. Also, mean spirometric measurements and serum ChE level were significantly decreased among pesticide-exposed workers (due to exposure to pesticides) than controls. At the same time, spirometric values decreased significantly with the increase in work duration in pesticides industry (due to prolonged exposure to pesticides). Moreover, there was a trend of reduction in the mean post- shift spirometric and serum ChE values than pre- shift ones among exposed workers (a temporary acute effect of occupational exposure to pesticides during the work shift). Moreover, there was a significant positive correlation between the reduction in mean levels of serum (ChE) among pesticide-exposed workers and reduction in the mean spirometric values. Therefore, it is recommended that:-

1- Clinical examination of the chest and spirometry should be included in pre employment and periodic medical examination for workers occupationally exposed to pesticides.

2- Environmental and personal hygienic measures should be applied strictly on the work environment and exposed individuals.

3. Further studies on wide scale to verify the results of this study.

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