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Original Research Article

Acute Health Effects of Pesticide Exposure among Farmers Directly Involved with Spraying: A Cross-Sectional Pilot Study from Kashmir Valley

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ABSTRACT

Background: Organophosphates (OP) are the extensively used pesticides that protect the agricultural produce from being damaged by the pests. These inhibit the acetylcholinesterase enzyme activity acutely which has a key role in the normal physiological functioning of the nervous system. There is an imminent possibility of deterioration of health in agricultural workers at the risk of OP exposure. The aim of this study was to analyze the clinical symptoms and chronic health effects of OP exposure among agricultural workers associated with spraying of pesticides in Kashmir, India.
Methods: This cross-sectional study was undertaken among agricultural workers associated with pesticide spraying at least once a year. A questionnaire based survey and clinical examination was conducted among study participants. The specific questions regarding the occupational history, pattern of spraying, history and symptoms of OP pesticide exposure were noted. The use of personal protective equipment, number of years of OP exposure and the volume of pesticide used were also noted. Biochemical evaluation and serum acetylcholinesterase levels were measured by standard protocol.
Results: A total of 63 subjects participated in the study with n= 61 (96.8%) males and n= 2 (3.2%) females. The study population had a mean age of 40.90 ± 12.66 years. Our results show considerable association between OP exposure and various neurological, psychological, mucoskeletal and respiratory symptoms, but it was not enough to provide evidence of biochemical derangement. The neurological symptoms included weakness (60.3%), dizziness (44.4%), headache (38.09%), fatigue (30.1%), and muscle pain (19.04%). The psychological symptoms included low mood (66.6%), anhedonia (46.03%), insomnia (23.8%), anxiety (19.04%), and nervousness (11.1%).Among respiratory symptoms cough (58.7%) was most commonly reported followed by cough with phlegm (41.2%) and breathlessness (12.6%). Only 9.5% of the study population reported the immediate symptom onset while 33.3% of participants reported delayed onset.
Conclusion: The neurological complications were most commonly reported followed by ophthalmological symptoms. We concluded that OP exposure affects the nervous system followed by musculoskeletal, integumentary and respiratory systems with least impact on cardiovascular system.

Keywords: organophosphorus; acetylcholinesterase; neurological; farm workers; occupational exposure; pesticides

INTRODUCTION

Pesticides are a broad range of chemical compounds that are used to kill pests, including insects, rodents, fungi and weeds [1,2] and are mainly used for crop protection, agricultural food production, and disease control. Organophosphates (OP) are widely used insecticides and are usually esters, amides or thiol derivatives of phosphoric, phosphonic or phosphinic acids. OPs acutely inhibit acetylcholinesterase enzyme affecting central nervous system and thus causing neurotoxicity and cell death [3].

The Union territory of Jammu and Kashmir has a total of 400 thousand hectares of land under cultivation as of financial year 2020[4].In the districts of Kashmir division about 60% of the total reporting area is under cultivation except in Ganderbal and Srinagar in which it is 47 and 49% respectively [5]. OP pesticides are commonly used in agriculture which may lead to high background exposure. In occupationally exposed individuals, spraying of pesticides has been associated with impaired neurological functions, impaired kidney function and detrimental effects on peripheral nervous system [6]. In non-occupationally exposed individuals, the exposure commonly occurs through ingestion food pretreated with pesticides [7] or by the use of insecticides in and around residential areas [8,9]. A number of animal studies suggest that cognitive changes, altered neuromotor/sensory function, impaired vestibular function, electrophysiological changes occur with the chronic use of pesticides[10,11]. In humans this may lead to cognitive alterations, affective disorders, psychomotor changes, altered motor function and changes in vibration sensitivity/nerve function[11–13].

Different animal studies have shown that suboptimal exposure of OP pesticide potentially changes the psychological [14]and neurochemical [15] behavior which can lead to cognitive impairments [16].It can also cause developmental changes in the neurons[17], induce oxidative stress[18,19]and affect the levels of thyroid hormone[20,21].

The primary mechanism of action of the organophosphates is the irreversible inhibition of the enzyme acetylcholinesterase (AChE) that hydrolyzes the neurotransmitter acetylcholine in both the peripheral and central nervous systems. This causes accumulation of acetylcholine at cholinergic synapses, leading to overstimulation of muscarinic and nicotinic receptors and hence neurotoxicity[22]. The widespread use of OP pesticides in the agricultural industry in Kashmir to control the insects, pests and fungus and to enhance the crop and fruit production is recognized as a major chemical health hazard for the orchard workers, residents and children by the direct contact and by polluting the aerial, soil and water environment[23]. The residual concentrations of these toxic chemicals in the farm workers lead to a variety of neurological dysfunctions[24,25]. The aim of this study was to evaluate the acute health consequences among agricultural workers at the risk of pesticide exposure.

MATERIALS AND METHODS

This prospective population-based cross-sectional study was conducted among the agricultural workers of the Kashmir valley. The data was collected from January 2020 to December 2020. The inclusion criteria included subjects aged over 18 years who were mainly involved in spraying pesticides in the household. A total of 63 agricultural workers were enrolled for the study. The study was approved by the Ethics Committee of Government Medical College, Srinagar (137/ GMC/ ETH/ ICM dated 28-05-2019) and was conducted in accordance with the ethical principles of the Declaration of Helsinki. All the participants were asked to provide an informed consent before enrolment. A baseline demographic data was collected on a well-structured proforma which included the data on nutritional habits, anthropometric measurements, history of farm activity and pesticide application, cropping structure, age, sex, smoking status and health-related behaviors by an attending clinician. A 5 ml blood sample was collected from each study subject for biochemical and acetylcholinesterase evaluation. The analysis of full blood biochemistry, and serum cholinesterase was done. Biochemical parameters include serum creatinine, urea, uric acid, bilirubin, total protein, blood glucose, complete blood count, and lipid profile etc. The study subjects were also interviewed for 24-hour dietary recall.

The organophosphorus pesticide exposure was measured using the amount (in kilograms) of the pesticides' active ingredients applied by agricultural workers. The participants were asked to provide information regarding all the pesticides including the chemical name, the active ingredient percentage(s), the amount and duration of each pesticide application (hours and time/week, respectively), width of the area of pesticide application (meter square), the completeness of personal protective equipment (head cover, goggle glasses, mask, hand gloves, clothes and boot), and the target crop.

Statistical analysis: All statistical analyses were performed using IBM SPSS Statistics version 20. The multiple linear regression analyses were used to evaluate the association between cholinesterase activity and parameters of organophosphate exposure and renal function and blood chemistry. A p value of < 0.05 was considered statistically significant.

RESULTS

A total of 63 individuals participated in the study with a mean age of 40.90 ± 12.66 years. Among these, 61 (96.8%) were male and 2 (3.2%) were female. Approximately half of the 36 (40.0%) participants reported using any pesticide for 20 years or more. Table 1 summarizes the demographic characteristics, and levels of pesticide exposures. The sample population applied an average of approximately 874.07 ± 1306.24 liters of organophosphorus pesticides per year. 71.4% of patients reported using pesticides for 3-8 hrs per day while 53.9% used <500 liters of pesticide during a particular season. 61.9% (n=39) of participants reported spraying of OPs on vegetable and 65.07% (n=41) consumed these sprayed vegetables within 7 days. Only 9.5% of the study population reported the immediate symptom onset while 33.3% of participants reported delayed onset. The history of cancer, chronic kidney disease, and neurological disorder was reported in 42.9%, 31.7% and 38.1% respectively.

Table 1: Baseline demographic characteristics and exposure levels of the study population

Variables	Exposed N=63 (%)
Age	63 (100)
Years of pesticide use	63 (100)
<10 years	3 (4.76)
10-20 years	24 (38.09)
>20 years	36 (40.0)
Number of days of pesticide use	
<7 days	33 (52.3)
7-15 days	4 (6.34)
>15 days	26 (41.2)
Hours per day of pesticide use	
<3 hrs	11 (17.4)
3-8 hrs	45 (71.4)
>8 hrs	2 (3.17)
Number of liters of pesticide used	
<500 Liters	34 (53.9)
500-1000 Liters	14 (22.2)
>1000 Liters	15 (23.8)
Vegetable Spray	
No	24 (38.09)
Yes	39 (61.9)
Consumption of Sprayed Vegetables	
<7 days	41 (65.07)
7-15 days	22 (34.9)
Symptom Onset	
None	36 (57.1)
Immediate	6 (9.5)
Delayed	21 (33.3)
History of Cancer	
No	61 (96.8)
Yes	2 (3.17)
Family History of Cancer	
No	36 (57.1)
Yes	27 (42.9)
History of Chronic Kidney Disease	
No	43 (68.3)
Yes	20 (31.7)
Family history of Chronic Kidney Disease	
No	37 (58.7)
Yes	26 (41.2)
History of Neurological Disorder	
No	39 (61.9)
Yes	24 (38.1)
Family history of Neurological Disorder	
No	36 (57.1)
Yes	27 (42.9)
History of Comorbidity	
No	21 (33.3)
Yes	42 (66.7)
History of Medication	
No	40 (63.5)
Yes	23 (36.5)
History of Surgery	
No	35 (55.6)
Yes	28 (44.4)

Table 2: Clinical manifestations of the exposed individuals

Variables	Exposed N=63 (%)
Route of Exposure	
Inhalation	31 (49.2)
Skin Exposure	46 (73.0)
Ingestion	1 (1.5)
All	11 (17.4)
General Symptoms	
None	8 (12.6)
Fatigue	38 (60.3)
GeneralBody-ache	13 (20.6)
Feverish	0 (0)
All	3 (4.76)
Skin	
None	7 (11.1)
Irritation	16 (25.3)
Redness	32 (50.7)
Itching	37 (58.7)
Rash	3 (4.7)
All	2 (3.1)
Eye	
None	4 (6.3)
Blurring	15 (23.8)
Itching	45 (71.4)
Redness	35 (55.5)
Watery	28 (44.4)
Decreased Vision	2 (3.17)
Respiratory	
None	7 (11.1)
Cough	37 (58.7)
Chest Pain	9 (14.2)
Wheeze	5 (7.9)
Sputum	1 (1.5)
Breathlessness	8 (12.6)
Phelgm	26 (41.2)
Cardiovascular	
None	24 (38.09)
Palpitations	19 (30.1)
Breathlessness	6 (9.5)
Chest Pain	2 (3.1)
Gastrointestinal	
None	9 (14.2)
Increased salivation	13 (20.6)
Cramps	0 (0)
Abdominal Pain	8 (12.6)
Constipation	26 (41.2)
Vomiting	5 (7.9)
Diarrhoea	6 (9.5)
Other	9 (14.2)
Neurological	
None	9 (14.2)
Asthenia	4 (6.3)
Tremor	4 (6.3)
Headache	24 (38.09)
Dizziness	28 (44.4)
Weakness	38 (60.3)
Abnormal Sensation	1 (1.58)
Seizures	1 (1.58)
Paraesthesia	3 (4.7)
Muscle Pain	12 (19.04)
Muscle Cramps	0 (0)
Fatigue	19 (30.1)
Loss of Consciousness	0 (0)
Flickering of muscles	0 (0)
Psychological	
None	9 (14.2)
Low Mood	42 (66.6)
Decreased Sleep	15 (23.8)
Loss of Interest	29 (46.03)
Decreased Concentration	5 (7.9)
Feeling Nervous	7 (11.1)
Irritability	0 (0)
Trembing hands	2 (3.1)
Sleeping	1 (1.5)
Anxiety	12 (19.04)
Depression	4 (6.3)
Musculoskeletal	
None	8 (12.6)
Swollen Joints	0 (0)
Painful Joints	12 (19.04)
Pain in Back	30 (47.6)
Pain in Legs	40 (63.4)
Pain in arms	19 (30.1)

The major route of exposure was reported to be skin (73%) followed by inhalation (49.2%). The most prominent symptom was fatigue reported in 60.3% of study population while general body ache was reported in only 20.6%. Among cutaneous symptoms itching was found in (58.7%) followed redness (50.7%), skin irritation (25.3%) and rash (4.7%). Itching in eyes was the most common (71.4%) feature among ophthalmological symptoms. Redness in the eyes was reported among 55.5% while watery eyes and blurring of vision was reported in 44.4% and 23.8% respectively. Cough was reported among 58.7% of study population while cough with phlegm was reported among 41.2%. Among cardiovascular symptoms palpitations was most common (30.1%) while among gastrointestinal symptoms constipation was most common (41.2%). Increased salivation was reported among 20.6% of subjects followed by abdominal pain (12.6%), diarrhea (9.5%) and vomiting (7.9%). The neurological symptoms included weakness (60.3%), dizziness (44.4%), headache (38.09%), fatigue (30.1%), and muscle pain (19.04%). The psychological symptoms included low mood (66.6%), anhedonia (46.03%), insomnia (23.8%), anxiety (19.04%), and nervousness (11.1%). The musculoskeletal symptoms included pain in legs (63.4%), backache (47.6%), and pain in arms (30.1%) and joint pain (19.04%). The neurological features were most commonly reported followed by ophthalmological complaints while cardiovascular system was least affected.

The mean age of the sample was 40.90 ± 12.66 years. The average number of years of pesticide use was 11.56 ± 6.76 and the mean number of days of pesticide use was 5.58 ± 4.77. The average hours per day of pesticide use was reported to be 4.17 ± 2.20 while the number of liters of pesticide use was 874.07 ± 1306.24. The mean acetylcholinesterase activity of study population was 14.36 ± 5.45 U/ml. The clinical characteristics of the study population are given in table 3. The baseline kidney function test of the participants reveal the mean urea, creatinine, uric acid and albumin to be 32.71 ± 13.23 mg %, 1.00 ± 0.29 mg %, 5.50 ± 1.61 mg % and 4.42 ±

0.57 gm % respectively. The mean total protein was 7.38 ± 0.75 g/dl. The liver function tests show an average serum glutamic-oxaloacetic transaminase (SGOT) to be 26.16 ± 9.45 IU/L. The mean serum glutamate-pyruvate transaminase (SGPT) was 31.97 ± 18.22 IU/L, alkaline phosphatase (ALP) was 93.85 ± 26.59 U/L and total bilirubin was 0.72 ± 0.69 mg/dl. The baseline blood biochemistry show that average hemoglobin of12.79 ± 1.28 g/dl, the mean red blood cells were 4.98 ± 0.67 $*10^6/\mu l$, white blood cells were 6.56 ± 1.76 $*10^3/\mu l$ and lymphocytes were 40.19 ± 9.25% in the study population. The mean cholesterol levels were 193.15 ± 45.96 mg/dl while high density lipoproteins (HDL) and low density lipoproteins (LDL) were 50.00 ± 24.43 mg/dl and 105.45 ± 29.55 mg/dl respectively. The mean triglycerides (TG) were 180.83 ± 99.29 mg/dl. The average blood glucose was found to be 104.91 ± 31.61 mg/dl.

Table 3: Clinical characteristics of the study population

Characteristics	Exposed N=63 (Mean ± SD)
Baseline Characteristics	
Age (yrs)	40.90 ± 12.66
Number of years of pesticide use	11.56 ± 6.76
Number of days of pesticide use	5.58 ± 4.77
Hours per day of pesticide use	4.17 ± 2.20
Number of liters of pesticide use	874.07 ± 1306.24
Clinical Characteristics	
Urea (mg%)	32.71± 13.23
Creatinine (mg %)	1.00± 0.29
Uric Acid (mg%)	5.50± 1.61
Albumin (gm%)	4.42± 0.57
SGOT (IU/L)	26.16± 9.45
ALP (U/L)	93.85± 26.59
SGPT (IU/L)	31.97± 18.22
Bilirubin Total (mg/dl)	0.72± 0.69
Total Protein (g/dl)	7.38± 0.75
BG Random (mg/dl)	104.91± 31.61
HB g/dl	12.79± 1.28
RBC ($*10^6/\mu l$)	4.98± 0.67
WBC ($*10^3/\mu l$)	6.56± 1.76
Lymphocyte (%)	40.19± 9.25
TC (mg/dl)	193.15± 45.96
HDL (mg/dl)	50.00± 24.43
LDL (mg/dl)	105.45± 29.55
TG (mg/dl)	180.83± 99.29
Acetylcholinesterase activity (U/L)	14.36 ± 5.45

DISCUSSION

In this study we reported the health consequences and identified determinants of occupational exposure to organophosphate pesticides in agricultural population of Kashmir valley. Our study reports that the use of organophosphate toxicity is associated with symptoms of sympathetic and parasympathetic over-activation[26]. We found that almost all agricultural workers had applied OPs sometime during their farming career. The toxicity symptoms of OP exposure are directly related to the amount and duration of organophosphate use. The study participants mostly presented with delayed toxicity.

In this study, we found that increased neurologic symptoms were associated with chronic exposure to OP pesticides which was in consonance with the previous studies [27,28]. The chief clinical neurological features were weakness, dizziness and headache which are attributed to the chronic effects of OP exposure on the peripheral [13] and central nervous systems [29]. The neurological manifestations of chronic OP exposure were both muscarinic and nicotinic in nature which is due to the inhibition of AChE[30]. The symptoms like chronic fatigue and irritability were the common presentation and various previous reports confirm these findings [31,32]. The acute ophthalmological cholinergic effects including itching of eyes, redness and blurring of vision could be attributed to the overstimulation of postsynaptic acetylcholine accumulation resulting from AChE inhibition by OP pesticides. These results are in accordance with various previous reports[33–35]. The psychological symptoms including low mood (n=42), loss of interest (n=29), decreased sleep (n=15), anxiety (n=12) and depression (n=4) have been reported. This is in consistent with previous studies that pointed to a positive link between the long-term low-level exposure to OP and the development of chronic neurotoxic and neuropsychological effects such as anxiety, depression, and problems with memory and concentration [36,37]. The prevalence of musculoskeletal symptoms including pain in legs (63.4%), followed by back (47.6%) and arms (30.1%) is due the inhibition of AChE enzyme through its covalent modification leading to excessive cholinergic stimulation on the nicotinic receptors[38]. A number of previous reports suggest that occupational exposure of OP and agricultural tasks in the paddy field may be associated with the increasing prevalence of mucoskeletalsymptoms[39–41]. The dermal effects including itching, redness and irritation and respiratory effects including cough, breathlessness, are most likely caused by local effects [42,43]. OPs have been known to affect the respiratory system by peripheral muscarinic actions on the airways, nicotinic actions on the muscles of respiration, effects on the medullary center in the brain and direct toxic effects on the alveolar-capillary membrane[44]. Various studies report similar findings, where chronic exposure to OPs has been associated with decreased lung function and a rise in respiratory symptoms[45–47]. The gastrointestinal symptoms including constipation, salivation, abdominal pain etc. is due to the accumulation of acetylcholine at muscarinic sites producing an increase in secretions and gastrointestinal motility[48,49]. The nervous system was the most affected system followed by musculoskeletal, integumentary and respiratory systems. The predominant mode of exposure in our study was dermal. Although most of the agricultural workers reported being aware of the hazards of pesticide exposure, there was no significant relationship between awareness and the use of protective gears. Table 3 shows the baseline clinical characteristics of the study population. The average AChE levels were within normal limits (14.36 ± 5.45) while 6 subjects presented with below normal levels and 10 subjects presented with above normal levels. The biochemical parameters did not show any derangement.

There are several strengths and limitations to be considered. Our study explored the chronic health effects of OP exposure in agricultural workers. The chronic and low dose OP exposure may not induce the observable clinical symptoms, but the sub-clinical damages often ignored in the previous studies may probably occur following pesticide exposure. However, compared to the previous studies, our study had a relatively small sample size which might not reflect the true association between OP exposure and clinical manifestations. Also, our study did not take into consideration the seasonal pattern of OP exposure.

CONCLUSIONS

In conclusion, occupational exposure to OP induces acute and chronic adverse health effects. The prevalence of neuropsychiatric, musculoskeletal and respiratory symptoms was associated with the cumulative chronic low-dose exposure to OP pesticides in the study population. The wide array of symptomology suggests the involvement of both central and peripheral nervous systems. Therefore, there is a need for community awareness about the toxicity symptoms of OP exposure. A better regulatory control of pesticide handling and use will reduce the burden of pesticide related hazardous health effects.

DECLARATIONS

Ethical approval

Ethical approval was obtained from the Institutional Ethics Committee of Government Medical College/Shri Maharaja Hari Singh (IEC-GMC/SMHS), in accordance with Indian Council of Medical Research (ICMR) guidelines. Institutional Ethical Registration Number:137/ GMC/ ETH/ ICM dated 28-05-2019.

Consent to participate

All study participants provided informed written consent prior to study enrolment.

Conflict of interest

The authors declare that there are no conflicts of interest.

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