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Original research

Epidemiology of organophosphate poisoning in the North of Iran

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Abstract

The use of pesticides as one of the main agricultural poles has been increased in Iran in recent years. Organophosphate poisoning has harmful the consequences for human health. This study present clinical and laboratory evidences on the patients exposed to agricultural insecticides poisoning and the cause of these poisons. We collected clinical data from the patients referred to Razi Hospital, Rasht, Iran who were poisoned with organophosphorus toxins. For this purpose, a checklist was prepared, and data were collected for 414 patients between 2011 and 2016. The results showed that the most cases of poisoning were men (73%) and about 27.2% of the patients was in the age group of 45-60 years (highest frequency in age groups). The most frequent symptoms were vomiting (65%), nausea (61%), abdominal pain (39%), and perspiration (27%). There was also a decrease in consciousness (16%) and sialorrhea (16%). Totally, 186 (46.2%) patients were exposed to organophosphorus toxins by respiratory and 215 (53.4%) orally. Out of the 414 samples, 102 (33%) had abnormal creatine phosphokinase (CPK) enzymes and 114 (34.5%) abnormal lactate dehydrogenase (LDH). Mean hospital length of stay (LOS) was 3.3 days. We found significant relationship of LOS with heart failure, hypertension, and addiction. To better manage the process of treatment of agricultural poisoned patients and to reduce the waste of limited resources available, careful consideration should be given to the type of pesticide used by the patient to prevent overdose and unintentional use of antidote.

Keywords: Organophosphate pesticides, Mortality, Poisoning, Length of stay, Guilan

1. Introduction

The application of insecticides has dramatically grown for agricultural development in low and middle income countries in the recent decades due to population growth. One of the most important side effects of increased use of pesticides is poisoning which could be very detrimental for human health and ecological balance. Poisoning account for about 0.15% of disability adjusted life years (0.17% in low income countries) and it is one of the leading causes of death [1]. In Iran, more than 3.7 million life-years of total population were lost due to poisoning [1]. Poisoning is also one of the major risk factors of hospitals admission in many countries. For example, about five million people are poisoned every year and receive health care services in hospitals in the United States [2]. Controlling pathogens and risk factors of diseases through the use of pesticides is very beneficial, but these toxins themselves might cause illness and death. These problems are caused by various direct and indirect exposures to pesticides. The prevalence of poisoning with chemical pesticides in developing countries is 13 times higher than in industrialized countries. It is estimated that about 85% of global

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pesticide productions are used in developing countries [3].

Frequent and unprotected contact with various types of insecticides cause risk of liver and kidney failure as well as cardiovascular disease and respiratory problems [4]. There is evidence that women who live in the environment with poisonous water have significant delay in intrauterine growth compare to others [5]. Studies also reported that parquet toxins, the oregano-phosphorus toxins, maneb and mancozib, lead to Parkinson's disease [6]. People living near areas exposed to insecticides are more likely to suffer Parkinson's disease [7]. Studies found that people who are exposed by herbicides are 4 times and those who are exposed by insecticides are 3 times more liked to suffer Parkinson [4, 8].

Organophosphorus compounds are one of the major pesticides used in agriculture and are responsible for more than 80% of poisoning with agricultural pesticides in Iran [9]. These compounds have become popular due to their effects as insecticides as well as low impact on environment and very low harmful radicals. They have been replaced by other insecticides, including organochlorines. These poisons are absorbed to body through the respiratory tract, digestive system, the mucosa, and skin. There are many types of organophosphate toxins in Iran, which are classified into high toxicity, moderate toxicity and low toxicity [10, 11].

In recent years, many solutions have been implemented to prevent and combat health-related problems of poisoning caused by exposure to organophosphates in Iran. In general, the best way to curb such poisonings is to educate general public, especially the farmers. Guilan province is one of the main centers of agricultural product and pesticide use, which has a higher rate of plant protection. Due to high population density in this province, the risk of exposure of people to such poisons is greater than other provinces. Therefore, the aim of this study was to provide with clinical and laboratory evidences about the patients exposed to agricultural pesticide poisoning, and the causes of these poisonings. We documented the situation in Guilan province and discussed ways to reduce the incidence of poisoning. The results of this study could be used for preventive and therapeutic implementations to reduce morbidity and mortality.

2. Materials and Methods

This was a cross sectional study included 414 patients referred to Razi Hospital of Rasht (Capital of Guilan province) between 2011 and 2016, diagnosed with an organophosphate poisoning problem. Razi hospital is the major and unique hospital for treating patients affected by poisoning. Majority of the poisoned people from all over of the province are referred for poisoning care in this hospital. In this study, we used data from health information system (HIS) and medical records of the patients. First, International Classification of Disease (ICD) codes of organophosphate poisoning was identified from the ICD book. This followed the extraction of next medical codes of target patients.

We developed a checklist to collect data. The checklist consisted of three parts. The first part included sociodemographic information the patients as age, sex, marital status, location, etc. The second part included information about disease and clinical records such as the history of underlying illnesses, addiction, drug use, and a history of suicide. The third part was on, clinical information such as increased body secretion, sweating, sore throat, tearing, bronchus, urinary incontinence, stool, nausea, diarrhea, mycosis and bradycardia as muscarinic symptoms, weakness, muscle cramps, fasciculation, respiratory paralysis, and tachycardia as signs of nicotine, as well as changes in the creatine phosphokinase (CPK) and lactate dehydrogenase (LDH) enzymes. Five researchers reviewed and revised the contents and design to validate the checklist. Data were collected by referring to the medical records department of Razi Hospital. Completed records were checked for the accuracy at first. After deleting incomplete and irrelevant samples (11 ones), data were entered to Excel software.

The ethical clearance was approved by the deputy research of Guilan University of Medical Sciences. We used descriptive statistics and regression models to analyze the data of study. All estimations were performed using Stata/SE software version 13.1 (StataCorp LP, TX, USA).

3. Results

Table 1 presents descriptive statistics of the patients included in this study. It shows that about 73% were male and 102 (25%) people were from urban regions. Totally, 96 (23%) people were not married.

The age distribution shows that 42 people (10%) were between 10-20 years old, 90 (22%) patients were between 20-30 years old, 99 ones (24.26%) were between 30-45 years old, 111 ones (27.21%) were was 42.89 (%16.97).

Figure 1 depicts the frequency of each clinical symptom among the poisoned patients. Vomiting (65%), nausea (61%), abdominal pain (39%), perspiration (27%), decreased consciousness (16%), and sialorrhea (16%) had the highest frequency of symptoms. In addition, 21 (5.19%) poisoned people died and 384 (94.81%) were treated. Furthermore, the frequency of exposure to poisoning is shown in the table 2. 186 people (46.27%) were exposed to Organophosphate pesticides from breathing, and 215 (53.48) were exposed to these toxins through eating. Only one person (0.25%) had exposure to the toxin through the eye.

Table 2 shows the status of the CPK and LDH enzymes in patients. Also, 207 (67%) of the samples had a normal CPK enzyme and for others CPK enzyme had increased. In addition, 216 patients had normal LDH (65.45%) enzyme and others had increase in LDH (34.45%) enzyme. Table 3 shows the prescription of atropine and pralidoxime in patients exposed to organophosphate pesticides. As outlined in the Table 3, for 240 (60.15%) patients atropine was prescribed and for 159 (39.85%) ones pralidoxime were prescribed for treatment; both of these drugs were prescribed for 111 (28%) patients. Table 4 shows that the average length of stay (LOS) of patients exposed to organophosphate pesticides was 3.30 days. The mean duration of LOS for atropine administration was 1.98 days and it was pralidoxime 2.07 days for pralidoxime. The difference in mean LOS between this two groups was statistically significant (P <0.001).

Table 1. Descriptive statistics of the participating patients

Variables	Frequency	Percentage
Female	111	27.21
Male	297	72.79
Living: urban region	102	25
Living: rural region	306	75
Not married	96	23.53
Married	312	76.47
Age		
10-20 years	42	10.29
20-30 years	90	22.06
30-45 years	99	24.26
45-60 years	111	27.21
60> years	66	16.18

Table 2. The status of the CPK and LDH enzymes in patients

Enzyme	Status	Frequency	Percentage
CPK	Normal	207	66.99
	Increased	102	33.01
LDH	Normal	216	65.45
	Increased	114	34.55

Figure 1. Frequency of clinical symptoms of patients exposed to organophosphate pesticides (total 414 patients).

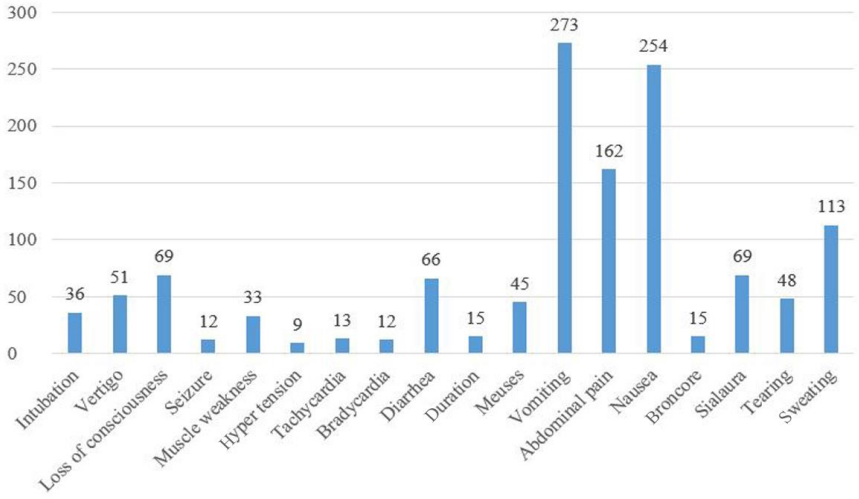

Table 3. Prescription of atropine and pralidoxime in patients exposed to organophosphate pesticides

Drug	Prescription	Frequency	Percentage
Atropine	Prescribed	240	60.15
	Not prescribed	159	39.85
Pralidoxime	Prescribed	159	39.85
	Not prescribed	240	60.15
Both	Prescribed	211	28.03

Table 4. The average length of stay of patients exposed to organophosphate pesticides

Variable	Length of stay	SD	Significant level
Atropine only	1.980	1.464	P <0.001
Pralidoxim only	2.067	1.893	
Total	3.303	2.816	

Results from the Poisson regression models on the relationship between individual, exposure and clinical factors of patients and hospital length of stay are presented in Table 5. There were no significant relationships of age, gender, exposure type with hospital length of stay. The incidence rate ratio (IRR) of health failure was 1.901 (P =0.000), indicated that poisoned people with heath failure stayed in hospitals about two times more than others. In addition, the patients suffering from addiction (IRR= 1.436), utilizing atropine (IRR= 1.404), having intubation (IRR= 2.189), and having hyper tension (IRR= 2.471), urinary incontinence (IRR= 1.797), sialorrhea (IRR= 1.335) and sweat (IRR= 1.303) had significantly higher length of stay in the hospital.

4. Discussion

The results of this study showed that nausea and vomiting were the most common clinical symptoms of the patients who were exposed to organophosphate

Table 5. Relationship between individual, exposure and clinical factors of patients and hospital length of stay

Variable	IRR	SE	P	95 % CI	
Age	1.002	0.003	0.519	0.996	1.008
Gender (Ref)	0.843	0.087	0.100	0.688	1.033
Exposure					
Gastrological	0.963	0.132	0.782	0.736	1.259
Underling disease					
Others	1.216	0.156	0.129	0.945	1.564
Diabetes	1.206	0.205	0.271	0.864	1.683
Heath failure	1.901	0.244	0.000	1.478	2.445
Addiction	1.436	0.177	0.003	1.128	1.829
Suicide	1.237	0.138	0.056	0.994	1.538
Pralidoxim	1.178	0.124	0.120	0.958	1.448
Atropine	1.404	0.133	0.000	1.165	1.691
CPK	1.000	0.000	0.378	0.999	1.000
LDH	1.000	0.000	0.180	1.000	1.001
Intubation	2.189	0.475	0.000	1.430	3.351
Vertigo	0.984	0.151	0.915	0.729	1.328
Loss of consciousness	1.093	0.143	0.497	0.846	1.413
Epilepsy	0.586	0.246	0.202	0.257	1.332
Weakness	1.041	0.152	0.782	0.782	1.388
Hypertension	2.471	0.614	0.000	1.518	4.023
Tachycardia	0.518	0.203	0.093	0.240	1.117
Bradycardia	0.621	0.179	0.098	0.353	1.092
Diarrhea	0.824	0.098	0.101	0.653	1.039
Urinary incontinence	1.797	0.384	0.006	1.182	2.730
Miosis	0.965	0.158	0.828	0.699	1.331
Vomiting	0.839	0.130	0.257	0.620	1.136
Abdominal pain	0.746	0.078	0.005	0.609	0.915
Nausea	1.317	0.195	0.063	0.985	1.760
Bronchorrhea	0.619	0.146	0.042	0.390	0.982
Sialorrhea	1.335	0.184	0.036	1.019	1.749
Tearing	0.831	0.127	0.224	0.616	1.120
Sweat	1.303	0.146	0.018	1.047	1.623
Constant	1.619	0.274	0.004	1.163	2.256

Note: IRR=Incidence rate ratio, SE=Standard error, and CI= Confidence Interval

pesticides. Abdominal pain and sweating were the next reported symptoms. Nausea, vomiting, and headache were found to be the most frequent symptoms of the patients in Yazd, Iran in 2012 [12]. Talaei et al. found that abnormal pulmonary sounds, meiosis, increased salivation, and vomiting were the most frequent in Tehran [8]. In addition, Shayeghi et al. concluded that headache, dizziness, and nausea had the highest frequency in patients' clinical symptoms [11]. In other studies, the most common complication of patients was nausea and vomiting and increased salivation and salivary secretion and the least complication was incontinence in the urine. Coughing, sputum excretion and wheezing were the highest prevalence in exposed pesticide pesticides [13-15]. Studies also found relationships between dizziness

and vomiting due to organophosphate toxicities and some cardiovascular symptoms such as low blood pressure, bradycardia, and arrhythmia, as these symptoms lead to a worse prognosis [16]. Therefore, severe complications and mortality could be increased in poisoned people if they are poorly tracked specially in patients suffering cardiovascular diseases.

Findings of ours study revealed that 5% of patients exposed to organophosphate toxins died. A study conducted in Khorramabad city of Iran found that about 7% died out of 153 exposed to organophosphate and oran glycerides, of which 3% were exposed to organophosphate pesticides [2]. In a study in Zanjan, it was found that 2 (3%) out of 57 children were exposed to organophosphate died [9]. Mean age of the exposed group was 42.89 years. Also, 45 and 60 years old group had the highest frequency of organophosphate poisoning. In a study conducted in Iran, the age group of 15 to 30 years was the most frequent people who exposed to organophosphate toxins. However, in a study conducted in Fasa, the average age of exposed individuals was 45.6 years old [2, 15, 17].

The findings of this study showed that 46% of the patients were exposed to inhalation and 53% were digested with toxin and only one had eye exposure. About 92% of exposures were deliberated and only 8% were unwanted in Mahmoudi study [2]. In another study, about 60% of the poisonings were respiratory, 23% ocular, and the rest were edible related to occupational poisoning [13]. In Mashhad, it was also found that 14% of the exposures were accidental, 5% were occupational and the rest were suicidal [10]. In Saudi Arabia, 69% of the cases were digested and 15% through inhalation and other exposed through the skin [18].

We found that about 33% of patients of the study had increased CPK enzyme and 35% had increased LDH enzyme. CPK is found primarily in muscle. In the serum, it increases when damage occurs to muscle cells. This enzyme usually increases six hours after the lesion. If the tissue lesion is not very serious, the enzyme level reaches its peak 18 hours later and returns to its normal level 2 to 3 days later. The activity of LDH in the cell is 500 in terms of its serum level, and since LDH is a cytoplasmic enzyme, it can be a sensitive marker for tissue damage [19, 20].

The findings revealed that the LOS in the hospital was 3.30 days. The mean LOS of atropine treated patients was 1.98 and pralidoxime administration was 2.06 days. On average LOS of the patients exposed to organophosphate pesticides was 6 days and 11 days in India and Japan, respectively [21, 22]. Priyendu et al., found that the LOS was 9 days in Saudi Arabia. The results from the regression model indicated the importance of chronic diseases management of organophosphate poisoning. Poisoned patients suffering hypertension, hearth failure, and addiction were more severe than others. This suggest that these people should have more notice than others [23].

Organophosphate pesticides have many usages. For example, it is used in agriculture and pest management in farms. Famers are exposed to this type of pesticides as well as pesticide producer factory workers [9]. Therefore, it is very important to use protective equipment and safety tools in these occupational group. Unfortunately, most of Guilanian farmers work in their own farms privately without any provision and control. Farming ministry could inform farmers about the dangers of exposure to organophosphate pesticides and can educate farmers about the ways of being protected from the dangers of organophosphate poisoning. It has been argued that poisoning of agricultural workers with pesticides, including organophosphorus pesticides, is more prevalent in less developed countries [24, 25]. In addition, this could lead to direct exposure to poisoning in famers and indirect effects on agricultural products consumer [26]. Therefore, training farmers in the proper use of the pesticides can be very effective. These types of trainings need between sectoral collaborations and ministry of health must alert other related organizations about the side effects of using these toxins. Meanwhile, checking the medical records of individuals during supply of the pesticides can be effective.

This study had some limitations. Firstly, there were missing in patients' information and biographies, and clinical history and prescribing drugs were illegible in some cases. In addition, we could not access data from other hospitals or cities in the province of Guilan, and the study was limited to the Razi hospital in Rasht. However, all patients in other hospitals were also transferred to Razi Hospital in Rasht.

Guilan province is a province covered by agricultural fields and there is a large amount of access to agricultural pesticides and organophosphates in the province. The share of agriculture work is high in this

province and there is increasing rate of toxins. Therefore, training of farmers to properly use these toxins as well as utilizing prohibiting equipment could be effective to lessen the harmful health effects.

Authors' contributions

HM, MY, EH conducted the study design. BF data collection. BF, MH data sorting and analysis. HM, MH, EH drafting the article. HM, MY, EH critical revisions. All authors read and approved the final version of article.

Conflict of interests

There is no conflict of interest.

Ethical declarations

The ethical clearance was approved by the deputy research of Guilan University of Medical Sciences (Registered no. 1987).

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