ORIGINAL ARTICLE

Factors affecting mortality in patients with organophosphate poisoning

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Abstract

Objective: To investigate the relationship between clinical and demographic characteristics and mortality in patients with organophosphate poisoning.

Methods: The retrospective study was conducted at Dicle University,Diyarbakir,Turkey, and comprised data of patients who presented with organophosphate poisoning between April 2004 and April 2013. The records were assessed in two groups, with Group 1 having data related to recovery, and Group 2 having data related to mortality. SPSS 16 was used for statistical analysis.

Results: Of the 296 patients, 219(74%) were women. Mortality was the outcome in 41(13.9%) cases. In Group 2, mean age, marital status, rural origin, presence of psychiatric disease, being illiterate, presence of nicotinic symptoms, and late admission were significantly higher than Group 1 ($p<0.05$ each). Logistic regression analysis indicated bradycardia as the most prominent independent predictor of mortality ($p<0.001$). Other independent predictors were age, glucose level, lactate dehydrogenase, coma and acidosis ($p<0.05$ each).

Conclusion: Independent predictors of mortality in patients with organophosphate poisoning as bradycardia, age, glucose, lactate dehydrogenase level and acidosis.

Keywords: Poisoning, Organophosphate, Mortality. (JPMA 65: 967; 2015)

Introduction

Organophosphate (OP) compounds have become the most widely used pesticides for agricultural pests throughout the world from the 1980s and the risk of acute and subacute toxicity is high in humans.[1] OP compounds are used as insecticides, pesticides, herbicides, and chemical battle agents.[2-4] OP compound's easy availability is accountable for increasing incidences of pesticide poisoning and it being a major reason of morbidity/mortality that poses public health problem in a developing territory.[5,6] It has been calculated by the World Health Organisation (WHO) that 3 million people are poisoned with OP, and 250,000 are killed every year, particularly in Asian countries.[7-11]

The widespread form of OP poisoning is suicidal attempt.[12-15] Intentional poisoning with OP was reported as 10-36.2% in developed countries, 40-60% in African countries and 65-79.2% in developing countries.[16-18] Coincidental exposure is more widespread in children and female housewives.[19,20] In previous studies, OP poisoning rate in patients presenting to the emergency department have been reported in the range of 34-39% in our country.[21,22]

In case of OP poisoning, the acetylcholine that accumulates due to the inhibition of the acetylcholinesterase enzyme may affect vital organs such as the sympathetic and parasympathetic ganglions, striated muscles, and the diaphragm and may cause life-threatening clinical conditions.[23] Clinical findings include nausea, vomiting, fatigue, dizziness, hyper-salivation, hyper-secretion and coma.[24] In OP poisoning, although mortality depends on the amount of the ingested substance, time of the treatment, respiratory support, intubation and separation from the ventilator, the mortality ratio varies between 3-25%.[25] Therefore, an early diagnosis and treatment is of utmost importance in OP poisoning in order to reduce mortality.

The current study was planned to investigate relationship between clinical and demographic characteristics and mortality in patients with OP poisoning, which is a condition frequently observed in Turkey.

Patients and Methods

The retrospective study was conducted at Dicle University, Diyarbakir,Turkey, and comprised data of patients who presented with OP poisoning between April 2004 and April 2013.The records were assessed in two groups, with Group 1 having data related to recovery, and Group 2 having data related to mortality. Age, gender, educational background, place of residence, marital status, season of presentation to the hospital, way and cause of the exposure to the substance, period of time between the exposure and the presentation, clinical findings at presentation, complete blood count, biochemical

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parameters, including glucose, urea, creatinine, sodium, potassium, chloride, aspartate aminotransferas (AST), alanine transaminase (ALT), lactate dehydrogenase (LDH) and creatine kinase (CK), arterial blood gases, electrocardiography (ECG) results, duration of the hospital stay, complications that developed during the follow-up, any underlying psychiatric disorders, clinical outcome, and cause of death were recorded. Patients whose data in the file could not be verified or was inadequate, or patients below the age of 15, were excluded.

During the initial evaluation in the emergency room, patients whose vital signs were stable and who had not received any treatment before presentation, were given activated charcoal following gastric lavage. Hypotensive patients (systolic blood pressure [SBP] < 90mmHg) received fluids and their urine output was monitored using a urinary catheter. Atropine was administered in repeated doses of 0.5-2mg until atropinisation findings, including reduced secretions, flushing, mydriasis and sweating, were observed. Following the 1gr loading dose, pralidoxime was administered as a 200mg/hour infusion. Patients who had ingested low doses of OP and those who did not develop hypotension (BP<90/60 mmHg), bradycardia (<60 bpm) and acidosis within the first 24 hours were discharged with due prescriptions, while the rest were followed up in the related clinics.

The patients were evaluated in terms of nicotinic and muscarinic symptoms and symptoms of the central nervous system (CNS). Hyper-salivation, hyper-lacrimation, increased bronchial secretion, hyperhidrosis, miosis, bradycardia, bronchospasm, abdominal pain and frequent urination were grouped as muscarinic symptoms. Paralysis, fasciculation, myasthenia, tachycardia (>100 bpm) and hypertension (BP>140/90 mmHg) were assessed as nicotinic symptoms. Headache, dizziness, confusion, psychosis, convulsion, coma, tremor, anxiety and respiratory depression were taken as symptoms related to the CNS.

Statistical analyses were done using SPSS 16. Parameters were shown as mean ± standard deviation or in terms of frequencies and percentages. Two-sided t-tests and Pearson's chi-square tests were used to analyse the differences in means and proportions between the groups. Logistic regression analysis was performed to evaluate independent predictors of mortality. The covariates included in the analysis were age, SBP, presence of acidosis, glucose, LDH, bradycardia, presentation in the spring, coma and the cause of OP intake. P<0.05 was considered significant.

Results

Of the 296 patients, 219(74%) were women. The overall mean age was 27.29±11.4 years (range: 15-69 years). Mortality was the outcome in 41(13.9%) cases. The cause of death was respiratory failure in 28(68%), cardiac arrest 8(20%), and renal failure 5(12%).

The mean age was significantly lower in Group 1(p<0.001), while the gender profile of both groups was similar (p>0.05).Illiteracy was higher in Group 2 (p<0.001). Also, the ratio of the patients originating from rural areas and those having psychiatric diseases was significantly higher in Group 2(p<0.05 each) (Table-1).

Number of patients conscious at presentation were significantly higher in Group 1(p<0.001), while those in coma were significantly more common in Group 2 (p<0.001). SBP of patients was similar in both groups, while the heart rates were higher in Group 2 (p<0.001). Blood glucose levels were also significantly higher in Group 2 (p<0.001). Blood gas tests revealed that the pH values were significantly lower in Group 2(p=0.001). ECG examination indicated significantly more frequent tachycardia in Group 2 (p<0.001), while bradycardia was more common in Group 1 (p<0.001) (Table-2).

Table-1: Demographic characteristics.

	Group 1 (Recovery) n=255	Group 2 (Mortality) n=41	Total n=296	p value
Age (Years)	26.13±10.5	34.54±15.26	27.29±11.4	<0.001
Female gender	191 (74.9%)	28 (68.3%)	219 (73.9%)	0.37
Married	107 (42%)	27 (65.9%)	134 (45.2%)	0.004
Rural origin	138 (54.1%)	33 (80.5%)	171 (57.7%)	0.002
Psychiatric disease	109 (42.7%)	5 (12.2%)	114 (38.5%)	0.001
Educational status				
Illiterate	77 (30.2%)	27 (65.9%)	104 (35.1%)	<0.001
Primary school	17 (6.7%)	3 (7.3%)	20 (6.7%)	0.87
High school	18 (7.1%)	3 (% 7.3)	21 (7.1%)	0.95
University	4 (1.6%)	0	4 (1.3%)	-

Table-2: Comparison of clinical and laboratory findings at presentation.

	Group 1 (Recovery) n=255	Group 2 (Mortality) n=41	Total n=296	p value
Consciousness				
Conscious	199 (78%)	6 (14.6%)	205 (69.2%)	<0.001
Confused/Lethargic	46 (18%)	9 (22%)	55 (18.5%)	0.55
Coma	10 (4%)	26 (63.4%)	36 (12.1%)	<0.001
ECG				
Normal	58 (22.8%)	3 (7.3%)	61 (20.6%)	0.02
Bradycardia	148 (58.0%)	5 (12.2%)	153 (51.6%)	<0.001
Tachycardia	45 (17.6%)	29 (70.7%)	74 (25%)	<0.001
ST-T change	4 (1.6%)	4 (9.8%)	8 (2.8%)	0.003
Systolic blood pressure (mmHg)	114.1±18.3	112.9±43.4	113.9±23.7	0.76
Heart rate (pulse/min)	80.1±18.9	97.7±34.9	82.56±22.6	<0.001
Blood glucose (mg/dl)	131.8±60.3	247.3±68.8	147.8±73.3	<0.001
Urea (mg/dl)	26.2±9.9	26.3±14.6	26.7±16.3	0.96
Creatinine (mg/dl)	0.79±0.2	0.87±0.2	0.8±0.2	0.04
Sodium (mmol/L)	136.7±3.7	138.0±5.0	136.9±4.0	0.06
Potassium (mmol/L)	3.6±0.4	3.4±0.4	3.58±0.4	0.005
Chloride (mmol/L)	102.0±5.2	105.5±5.6	102.5±5.4	<0.001
ALT (U/L)	21.6±11.9	35.3±38.6	23.5±18.6	<0.001
AST (U/L)	21.5±8.9	41.4±55.3	24.3±23.0	<0.001
LDH (U/L)	286.1±119.7	415.6±123.4	304±128.1	<0.001
CK (U/L)	148.5±213.4	217.6±202.6	158.1±212.9	0.054
pH	7.36±0.05	7.20±0.14	7.33±0.1	0.001

ECG:Electrocardiography. ALT:Alanine transaminase. AST:Aspartate aminotransferas. LDH: Lactate dehydrogenase. CK:Creatine kinase.

Table-3: Main characteristics of intoxication.

	Group 1 (Recovery) n=255	Group 2 (Mortality) n=41	Total n=296	p value
Cause of intake				
Accident	38 (14.9%)	3 (7.3%)	41 (13.8%)	0.19
Suicide	217 (85.1%)	38 (92.7%)	255 (86.1%)	
Intake route				
Oral	230 (90.2)	38 (92.7%)	268 (90.5%)	0.61
Skin	38 (14.9%)	6 (14.6%)	44 (14.8%)	0.96
Inhalation	32 (12.5%)	0	32 (10.8%)	-
Season				
Autumn	66 (25.9%)	17 (41.5%)	83 (28%)	0.03
Spring	87 (34.1%)	7 (17.1%)	94 (31.7%)	0.03
Summer	25 (9.8%)	3 (7.3%)	28 (9.4%)	0.61
Winter	4 (1.6%)	0	4 (1.3%)	-
Nicotinic symptoms	97 (38%)	35 (85.4%)	132 (44.5%)	<0.001
Muscarinic symptoms	230 (90.2%)	38 (92.7%)	268 (90.5%)	0.61
Symptoms of the central nervous system	77 (30.2%)	38 (92.7%)	115 (38.8%)	<0.001
Time until presentation (Hours)	2.95±3.67	4.41±2.34	3.15± 3.19	0.014

The cause and intake route showed a similar distribution in both groups, although the time until presentation was longer in Group 2 (p=0.014). Nicotinic symptoms and symptoms of the CNS were significantly more frequent in Group 2 (p<0.05) (Table-3).

Logistic regression analysis indicated bradycardia as the most prominent independent predictor of mortality (p<0.05). Other independent predictors were age, glucose level, LDH, coma and acidosis (p<o.05 each) (Table-4).

Table-4: Independent predictors of mortality.

Variable	Odds ratio	95% CI	p value
Age	1.053	1.012-1.096	0.01
Glucose	1.022	1.014-1.030	<0.001
LDH	1.004	1.000-1.008	0.033
Bradycardia	12.652	3.123-51.255	<0.001
Coma	5.201	1.754-15.425	0.003
Acidosis	3.742	1.010-13.864	0.04

CI: Confidence interval
LDH:Lactate dehydrogenase.

Discussion

Our study demonstrated that the independent predictors of mortality in OP poisoning are age, bradycardia, glucose level, LDH, coma and acidosis. While our study reports a mortality rate of 13.9%, in literature the ratio varies between 3-25% depending on various factors.[26]

In various studies, the time until the presentation has been underlined as an important parameter. In one study, the mean time lapse was reported as 4 hours.[27] Another study found it to be 3.45 hours, but it did not observe any significant difference between the mortality and survival groups.[28] In our study, the mean time until presentation to the hospital following the exposure to the substance was 3.15±3.19 hours. Also, the time until presentation to the hospital was significantly shorter in Group 1. However, logistic regression analysis did not point out the time period until presentation to the hospital as an independent predictor of mortality.

In one study, the mean age of patients was found to be 39.4 years,[29] while in another study it was 32.2 years.[30] In our study, the mean age was 27.29±11.4 years and the patients who survived were observed to be younger. In addition, the age has been found to be an independent predictor of mortality. This may be associated with increased accumulation of the substance in the body in parallel to the increased volume of the fat tissue with advancing age and the slower metabolism of the substances in the liver. Also, the tendency to respiratory failure, which is an important cause of mortality, increases with age.

One study has demonstrated that the cases tend to accumulate during the spring and summer months.[31] Our study has shown that the prevalence of OP poisoning generally increases during the spring and autumn. Also, the incidents in our study were observed to increase during spring in Group 1 and during autumn in Group 2. This may be associated with accidental exposure to the substance in patients who present during spring (since herbicides and pesticides are frequently used in this season), while the intake in autumn may be associated with suicide (due to the increase in depressive attacks).

In one study, pH values of patients were observed to be similar among those who survived and those who died.[32] However, in the same study, the pH values were significantly lower among those who had respiratory failure in comparison to those without respiratory problems (7.3 ± 0.2 vs. 7.4±0.1, respectively; p=0.04). In a study,[33] the pH value of the cases that resulted in death was significantly lower and a pH<7.2 was found to be an independent predictor for mortality (OR:10.1, CI:2.37-42.59,p=0.002). In our study, the pH value of the patients who died was significantly lower than those who survived. In addition, the presence of acidosis was observed as an independent predictor of mortality (OR:3.7, CI:1.010-13.864, p=0.04).

The mechanism of the changes in the ECG in patients poisoned with OP is yet to be cleared. Sympathetic and parasympathetic over-activity, hypoxia, acidosis, electrolyte disturbances, and direct toxic effects on the myocardium have been suggested as possible mechanisms.[34] A study described three phases of the cardio-toxicity that develops subsequent to OP poisoning. Phase 1 is characterised by a brief period of increased sympathetic tone; in phase 2, a prolonged period of parasympathetic activity is observed; and phase 3 involves Q-T prolongation followed by ventricular arrhythmia.[35] In a study, ECG findings of 37 patients who presented with OP poisoning were investigated.[36] Sinus tachycardia was observed in 15(40.5%), sinus bradycardia in 7(18.9%) and ST-T changes were detected in 11(29.7%) patients. Another study observed abnormal ECG findings in 23.5% patients.[30] The most commonly observed ECG finding was tachycardia with a 32.9% ratio. Our study included relatively more patients and the most frequently observed ECG change was sinus bradycardia (51.6%). No abnormal ECG findings were observed in 20.6% patients. This result is also in line with the fact that the muscarinic symptoms were the dominant symptoms in our patients. The variations in the frequency of tachycardia and bradycardia between the studies may be associated to the differences in the time until presentation to the hospital. Following the exposure to OP, initially tachycardia is observed due to sympathetic activation, which is followed by bradycardia due to parasympathetic activation. Thus, bradycardia is observed more frequently in patients who present later to the hospital and this finding is strongly associated with mortality. In our study, bradycardia was observed to be the strongest independent predictor of mortality.

Serum glucose levels in patients with OP poisoning have been investigated in various studies.[29,37,38] In one such study, the mean glucose level was 144 mg/dl and it was determined to be an independent factor in the development of the intermediate syndrome.[29] The intermediate syndrome is a clinical condition characterised by a paralysis in the respiratory muscles, weakness in the proximal limb muscles, and motor cranial nerve involvement in OP poisoning and it leads to a poor clinical outcome.[39,40] Another study pointed out a mean glucose level of 145mg/dl and 67.7% patients had hyperglycaemia. In our study, the mean glucose value was 147.8±73.3 mg/dl and it was found as an independent predictor of mortality. Hyperglycaemia in OP poisoning is generally associated with the catecholamine discharge from the adrenal medulla.[37]

In our study, there was no constant, and amount of OP ingested was missing because of limited data in patient files.

Conclusion

Independent predictors of mortality in patients with OP poisoning were found to be bradycardia, age, glucose, LDH level and acidosis. Keeping an eye on these parameters in detecting high-risk patients in the emergency room may contribute to low mortality.

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