Retrospective Analysis of Organophosphate Poisonings in an Intensive Care Unit in Turkey: A Single-Center Study

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Keywords

Organophosphates · Poisoning · Intensive care unit · Mortality · Toxicity

Abstract

Background: Organophosphates (OP) are frequently used as pesticides around the world in agriculture. Exposures to OP cause a significant number of poisonings each year and lead to deaths. Acute toxicity manifests as cholinergic crisis with glandular secretions, myasthenic-like syndrome, peripheral neuropathies, neuropsychiatric abnormalities, extrapyramidal disorders, altered mental status, and weakness.

Summary: After Institutional Review Board approval, this retrospective study was performed by evaluating the hospital records of patients admitted to an intensive care unit with acute OP poisonings. Data regarding age, gender, duration of hospitalization, severity, complications, and outcome of the patients were recorded. The data were presented as mean $\pm$ standard deviation, analyzed with SPSS software. A total of 47 patients were included in the study of whom 70.2% were female and 29.8% were male. Mean age of the patients was 25.8 years. The reason for poisoning was suicide in 80.9% and accident in 19.1%. Mean intensive care unit stay

was 5.9 days. The mortality rate was 12.8%. **Key Messages:** Our study contributes substantial information regarding the epidemiology and outcomes of acute OP poisonings in a tertiary care training hospital in a rural area; its relatively small sample size and its being a retrospective record-based study are limitations of the study. There is a need for future studies to reveal the underlying factors responsible for acute OP poisonings in Turkey and accordingly to solve these problems and thereby reduce the incidence of acute OP cases.

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Introduction

Since Turkey is an agriculture-based country, organophosphates (OP) still remain the main agent for crop protection and pest control and therefore harm people who are overexposed accidentally while handling the pesticides [1, 2]. Due to the low cost and easy availability, they have also become an agent of choice for suicide and self-poisoning. Frequently used OP include malathion, parathion, chlorpyrifos, diazinon, dichlorvos, fenitrothion, tetrachlorvinphos, and azinphos-methyl [3–5].

Table 1. Demographic characteristics of 47 patients poisoned with organophosphate

Age, years	
Mean $\pm$ SD	25.8 $\pm$ 11.8
Range	16–68
Gender, <i>n</i> (%)	
Male	14 (29.8)
Female	33 (70.2)
Exposure, <i>n</i> (%)	
Accident	9 (19.1)
Suicide	38 (80.9)
Ingestion, <i>n</i> (%)	
Oral	45 (95.7)
Inhaler	2 (4.3)
Mortality, <i>n</i> (%)	
Dying	6 (12.8)
Healing	41 (87.2)

Table 2. Intensive care tanks of 47 patients poisoned with organophosphate

Features	Average	SD	Min–max	<i>p</i>
Intensive care time, days	5.9	5.4	1–25	0.55
APACHE II score	18.31	9.15	5–45	0.036
Glasgow Coma Scale score	10.91	4.28	3–15	0.034
Mechanical ventilation duration, days	2.02	3.26	0–12	0.63

OP compounds inhibit acetylcholinesterase, and this results in the accumulation of acetylcholine with the overstimulation of cholinergic synapses. Clinical signs and symptoms depend on the nature of the OP compound, the amount consumed, time lapse between exposure and admission to the hospital, and the severity [4, 5].

The most lethal complication following OP poisoning is respiratory failure. This may have many reasons like aspiration of gastrointestinal contents, excessive secretions, neuromuscular involvement, intermediate syndrome, septicemia, and adult respiratory distress syndrome. In severe OP poisoning, early recognition of respiratory failure, fast endotracheal intubation, and mechanical ventilation can be life-saving [6]. These patients need intensive care management for respiratory and close hemodynamic monitoring due to the above-mentioned reasons.

With early diagnosis and treatment, the majority of OP poisonings could have been prevented and in many

studies high mortality rates have been reported following OP poisoning. There is a significant improvement, in general for critical care of the patients in recent years, and we would like to determine the effect of general critical care improvements on OP poisoning patients in Turkey.

Materials and Methods

This retrospective study was conducted in the Dicle Medical University in Diyarbakır, Turkey. After Institutional Review Board approval, hospital records of patients with acute poisoning from the years 2006 to 2011 were reviewed. All data were collected from the patients' charts. Totally 47 patients were included in this study. As per the case file, the diagnosis depended on the information received from either the patients or their family about the history of the exposure, contact, and characteristics of the clinics. Treatment was started as per the protocol for poisoning. After removing the clothes, the body was washed with soap. A nasogastric tube was inserted for gastric irrigation and decompression of the stomach. Patients with early symptoms were treated by stomach irrigation, maintenance of the fluid-electrolyte balance, forced diuresis, and the administration of activated charcoal. Patients requiring ventilatory support were intubated and managed as per the intensive care unit (ICU) protocols. Initial management of all patients with pralidoxime (PAM) and atropine was done as per the recommended dosage schedule. A starting loading dose of 1–2 mg of atropine was administered. A maintenance dose of 0.5–2 mg was repeated depending on the severity of the poisoning. An intravenous loading dose of 1,000 mg PAM was administered. The infusion dose of 4 mg/kg/h PAM was infused for 48 h. The total PAM and atropine doses given were recorded.

Demographic and routine laboratory results were recorded for the duration of the patients' stay in the ICU. Data related to a number of clinical outcomes such as Glasgow Coma Scale (GCS) on admission to the Emergency Department, Acute Physiology and Chronic Health Evaluation II (APACHE II) scores on entry to the ICU, duration of mechanical ventilation, and length of ICU stay, clinical findings, the way of exposure, and hospital stay were also recorded.

All data were analyzed with SPSS software, version 18.0. A detailed multiple-variable database was formed. Statistical comparisons were carried out using the Mann-Whitney U test and Student's *t* test. The Pearson test was used to evaluate correlations among variables. *p* values of 0.05 or less were considered to be statistically significant.

Results

During the study period, 47 patients with OP poisonings were admitted to our ICU. The mean age of all patients was 25.8 years. Of the 47 patients, 33 (70.2%) were female and 14 (29.8%) were male (Table 1; Fig. 1). The reason for poisoning was a suicide attempt in 38 patients (80.9%) and accidental exposure in 9 patients (19.1%)

Fig. 1. Gender distribution.

Fig. 2. Reason for poisoning.

Fig. 3. Route of exposure.

Fig. 4. Mortality rate.

(Fig. 2). One patient was poisoned through inhalation, while the gastrointestinal route of exposure was found in 46 (95.7%) (Fig. 3). Twenty-one patients were intubated and mechanically ventilated. The mean duration of mechanic ventilation was 2.02 days. Twenty-six patients were followed up with oxygen masks. Of the 21 patients ventilated, 10 were extubated after 48 h. The median GCS score on admission to the ICU was 10.9. For 3 of them, the GCS score was 3, whereas the GCS score was 15 for 19 of them. The median APACHE score was 18.3 (Table 2). The highest score was 45, while the least was 5. Six patients died in the ICU (Fig. 4). Twenty-two patients were oriented and cooperated, 12 of them were confused, and 13 of them were noncooperative. The mean ICU stay was 5.9 days (range 1–25). Forty patients were discharged after 1 week, 2 patients after 2 weeks, 4 patients after 3

Table 3. Clinical characteristics of 47 patients poisoned with organophosphate

Features	Yes, <i>n</i> (%)	No, <i>n</i> (%)
Muscarinic symptoms		
Myosis	29 (61.7)	18 (38.3)
Bronchial hypersecretion	24 (51.1)	23 (48.9)
Diarrhea	3 (6.4)	44 (93.6)
Salivation	39 (83)	8 (17)
Bradycardia	18 (38.3)	29 (61.7)
Nicotinic symptoms		
Fasciculations	32 (68.1)	15 (31.9)
Tachycardia	15 (31.9)	32 (68.1)
CNS symptoms		
Consciousness is OK	22 (46.8)	–
Confusion	12 (25.5)	–
Coma	13 (27.7)	–

Fig. 5. Muscarinic symptoms.

Fig. 6. Nicotinic symptoms.

Fig. 7. CNS symptoms.

weeks, and 1 after 4 weeks. The most frequent clinical findings were salivation (83%), fasciculation (68.1%), myosis (61.7%), hypersalivation (51.1%), bradycardia (38.3%), and tachycardia (31.9%) (Table 3; Fig. 5–7). Leukocytosis, hyperglycemia, and high levels of lactate dehydrogenase were observed on admission in laboratory findings (Table 4).

Discussion

This retrospective study underlines that OP poisoning is predominantly suicidal and affects primarily the young female population. OP compounds are used worldwide in agriculture in developing countries, and due to its easy

availability this leads to an increase in suicidal and accidental poisoning.

Diagnosis of OP poisoning depends on clinical presentation, history, and levels of cholinesterase levels. In our hospital, we started treatment immediately without waiting for the results.

The average age in our study was 25.8 years (range, 18–68). The demographic data in Turkey showed that the ratio of patients aged 35 or younger was 71.2–82%. Alpay et al. [7] showed in their study that the mean age was 20.9 years. Karalliedde [8] and Karalliedde et al. [9] reported a ratio of 78% of patients aged younger than 30. Many studies have reported female predominance with respect to OP intoxication as also seen in our study.

Table 4. Laboratory findings of organophosphate poisoning cases

Results	Average	SD	Min-max
WBC, $\times 1,000/\text{mm}^3$	14.2	6.07	1.4–32.7
Hemoglobin, g/dL	13.2	2.1	6.7–17.4
PLT, $\times 1,000/\text{mm}^3$	286	78.1	147–522
Urea, mg/dL	29.08	14.1	12–90
Creatinine, mg/dL	0.82	0.47	0.5–2.7
Sodium, mEq/L	138	5.8	122–166
Potassium, mEq/L	3.7	0.7	2.4–7
Calcium, mg/dL	8.7	0.8	6.4–10.4
Glucose, mg/dL	125.3	54.7	52–301
Amylase, U/L	108.9	112.8	33–557
Albumin, mg/dL	3.4	0.7	1.7–4.7
SGPT (ALT), IU/L	36.1	73.06	3–428
SGOT (AST), IU/L	50.8	130.7	6–913
PaO ₂ , mm Hg	94.4	32.1	40–176
PaCO ₂ , mm Hg	37.6	8.9	18–68
O ₂ saturation	91.2	10.6	52–99
pH	7.32	0.16	6.73–7.53

It was observed that of the patients admitted to the ICU, female patients made up 70.2% and suicide was the most common cause [10]. The possible reasons for this in our country might be unemployment and emotional problems in this young population.

The most common way of OP poisoning was found to be oral intake (95.7%). Yürümez et al. [11] reported a ratio of oral intake of 86.8%, while according to Alpay et al. [7] it was 97%, according to Özcan et al. [12] it was 91%, and according to Kavalcı et al. [13] it was 75.2%. This might be explained by its easy availability.

In the present study, all patients received PAM within 6–8 h of poisoning and required mechanic ventilation of 2–15 days. Respiratory depressions developed in these patients due to the aspiration of the gastric contents and secretions, thoracic muscle weakness and complications. The mortality rate was 12.7% in our study. Hussain and Sultan [14] reported 50% mortality in mechanically ventilated patients. Mortality increases in ICU patients requiring mechanical ventilation for more than a week. Lung complications, acute renal failure, and sepsis develop in these patients because of the prolonged ventilation and the severity of poisoning.

Antagonizing the actions of OP at muscarinic receptor sites is the target treatment for poisoning. It is administered every 10 min in doses of 2 mg. PAM is a compound which reactivates acetylcholinesterase from the OP-cholinesterase complex. Its main effect is on nicotinic, mus-

carinic and central nervous system receptors. It should be administered as soon as possible for beneficial response. All our patients received PAM for less than 8 h.

The duration of the mechanical ventilation was 2.02 days. In our study, these patients developed respiratory failure due to aspiration, thoracic weakness, pneumonia, and sepsis.

The mortality rate in our study was 12.8%. Hussain and Sultan [14] reported 8% mortality in patients who received mechanical ventilation. The patients who require mechanical ventilation for more than a week have high mortality rates depending on the severity of poisoning (33%).

The average dose of PAM used in our study was 32.5 g. The daily dose of PAM is nearly 10–12 g.

In a study, Lee and Tai [15] stated a relation between APACHE II score and OP poisoning. In our study, we found a mean APACHE II score of 18.3. There is a positive correlation between mortality and APACHE II scores. In OP poisoning, the APACHE II score has a prognostic value.

In this present study, the GCS score was found to be 10.91. GCS score is a good predictor for OPs ($p < 0.001$).

Laboratory findings can change in OP poisonings. Hyperglycemia can usually be seen with the release of catecholamines. Leukocytosis is common. In our study, amylase and leukocytes were found to be high. We also found urea and creatinine values to be high. The high scores were related with the mortality scores.

There is not a single significant association with death and OP poisoning. We assume that death due to OP poisoning is rather due to the more severe poisoning and the duration of the mechanical ventilation. The mortality can also be very high in case the victims are from rural areas in Turkey. We believe no single factor is responsible for mortality in these patients.

Conclusion

OP insecticide is also chosen for self-poisoning due to its low cost and easy availability. Mortality depends on the severity of poisoning, duration of the mechanical ventilation, and ICU stay, as well as the delay in starting medical treatment. There is a need for prospective studies to understand the underlying socioeconomic factors responsible for acute OP poisoning in our population, and, accordingly, address the problems to reduce the incidence of acute OP poisoning cases.

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Statement of Ethics

The authors have no ethical conflicts to disclose.

Author Contributions

A.İ.S.: Data collection and analyzing. E.T.K.: Writing the text and revising. M.S.A.: Data collection and revising. G.Ö.K.: Revising.

Disclosure Statement

The authors have no conflicts of interest to declare.

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