

EVALUATION OF PATIENTS WITH ORGANOPHOSPHATE POISONING IN THE EMERGENCY DEPARTMENT: A RETROSPECTIVE TWO-CENTER STUDY

ACİL SERVİSTE ORGANOFOSFAT ZEHİRLENMESİ OLAN HASTALARIN DEĞERLENDİRİLMESİ: İKİ MERKEZLİ RETROSPEKTİF BİR ÇALIŞMA

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Citation/Atf: Vural A, Dolanbay T, Şahin L, Altay MC, Canbaz H. Evaluation of patients with organophosphate poisoning in the emergency department: A retrospective two-center study. Journal of Advanced Research in Health Sciences 2024;7(2):87-92. <https://doi.org/10.26650/JARHS2024-1404063>

ABSTRACT

Objective: The widespread use of organophosphates (OP) as pesticides in global agriculture, pose significant health risks in both developing and industrialized nations. Exposure through ingestion, occupational contact, and suicide attempts leads to high morbidity and mortality. This study will retrospectively analyze the demographic, clinical, and laboratory characteristics of adult patients aged 18 years and older who presented to emergency departments.

Material and Methods: The study is a two-center retrospective analysis of the Niğde Ömer Halisdemir University Training and Research Hospital, Clinic of Emergency Medicine and Kafkas University Health Practice and Research Hospital, Clinic of Emergency Medicine. Patient data, including demographics, clinical details, and laboratory parameters, were recorded. Analysis covered routine blood tests, pseudocholinesterase levels, and electrocardiography findings. Patients diagnosed with OP poisoning (international classification of diseases (ICD) code T60.0) between 15 June 2020 and 15 June 2023 were included in the study.

Results: The study included 24 patients meeting inclusion and exclusion criteria. Oral exposure (41.7%) and inhalation (25%) were common routes. The hospitalization rate was 91.7%, with only 4.2% requiring intubation. No in-hospital mortality occurred. Pseudocholinesterase levels correlated negatively with pH, bicarbonate, anion gap and positively with c-reactive protein (CRP). Duration of hospital stays was negatively correlated with Glasgow coma scale (GCS), pH, bicarbonate, and positively correlated with the anion gap.

Conclusion: This retrospective, two-center study provides comprehensive insights into the demographic profiles, clinical manifestations, and treatment outcomes of adult patients presenting with OP poisoning in emergency departments. In our study, most organophosphate poisonings were accidental. In this respect, it is important to provide safety equipment, safe farming conditions, limited access to hazardous substances, emergency education, public health campaigns and safe work practices in factories and farms to prevent organophosphate poisoning. Furthermore, this study underlines the importance of assessment of clinical parameters such as GCS, pH and HCO₃ in predicting the severity and duration of hospitalization.

Keywords: Organophosphates, poisoning, mortality, biochemicals markers

ÖZ

Amaç: Organofosfatların (OF) küresel tarımda pestisit olarak yaygın kullanımını hem gelişmekte olan hem de sanayileşmiş ülkelerde önemli sağlık riskleri oluşturmaktadır. Yutma, mesleki temas ve intihar girişimleri yoluyla maruz kalma, yüksek morbidite ve mortaliteye yol açmaktadır. Bu çalışma, acil servislere başvuran 18 yaş ve üzeri yetişkin hastaların demografik, klinik ve laboratuvar özelliklerini retrospektif olarak analiz etmeyi amaçlamaktadır.

Gereç ve Yöntem: Çalışma, Niğde Ömer Halisdemir Üniversitesi Eğitim ve Araştırma Hastanesi, Acil Tıp Kliniği ve Kafkas Üniversitesi Sağlık Uygulama ve Araştırma Hastanesi, Acil Tıp Kliniği tarafından gerçekleştirilen iki merkezli retrospektif bir analizdir. Demografik bilgiler, klinik ayrıntılar ve laboratuvar parametreleri dahil olmak üzere hasta verileri kaydedilmiştir. Analizler rutin kan testlerini, psödokolinesteraz düzeylerini ve elektrokardiyografi bulgularını kapsamaktadır. Çalışmaya 15 Haziran 2020 ile 15 Haziran 2023 tarihleri arasında OF zehirlenmesi (uluslararası hastalık sınıflandırması (ICD) kodu T60.0) tanısı alan hastalar dahil edilmiştir.

Bulgular: Çalışmaya dahil edilme ve dışlanma kriterlerini karşılayan 24 hasta dahil edilmiştir. Hastaneye yatış oranı %91,7 olup sadece %4,2'si entübasyon gerektirmiştir. Hastane içi mortalite görülmemiştir. Psödokolinesteraz düzeyleri pH, bikarbonat, anyon açığı ile negatif; CRP ile pozitif korelasyon göstermiştir. Hastanede kalış süresi Glasgow koma skalası (GKS), pH, bikarbonat ile negatif; anyon açığı ile pozitif korelasyon göstermiştir.

Sonuç: Bu retrospektif, iki merkezli çalışma, acil servislere OF zehirlenmesi ile başvuran yetişkin hastaların demografik profilleri, klinik bulguları ve tedavi sonuçları hakkında kapsamlı bilgiler sunmaktadır. Çalışmamızda organofosfat zehirlenmelerinin çoğu kaza sonucu meydana gelmiştir. Bu açıdan, organofosfat zehirlenmelerini önlemek için fabrikalarda ve çiftliklerde güvenlik ekipmanları, güvenli tarım koşulları, tehlikeli maddelere sınırlı erişim, acil durum eğitimi, halk sağlığı kampanyaları ve güvenli iş uygulamaları sağlamak önemlidir. Ayrıca bu çalışma, GKS, pH ve HCO₃ gibi klinik parametrelerin değerlendirilmesinin hastaneye yatış şiddeti ve süresinin öngörülmesindeki öneminin altını çizmektedir.

Anahtar Kelimeler: Organofosfatlar, zehirlenme, ölüm, biyokimyasal belirteçler

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Submitted/Başvuru: 12.12.2023 • **Revision Requested/Revizyon Talebi:** 21.12.2023 • **Last Revision Received/Son Revizyon:** 21.12.2023

• **Accepted/Kabul:** 25.12.2023 • **Published Online/Online Yayın:** 26.04.2024



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INTRODUCTION

Organophosphates (OP) are chemical compounds commonly used in agriculture and known as pesticides (insecticides, herbicides, and rodenticides). Although poisoning from these substances is more common in developing nations, it is also a significant issue in industrialized nations (1-3). Accidental ingestion (oral), occupational exposure (through skin and inhalation) while working with pesticides, and unfortunately, suicide attempts are frequently observed. OPs are chemical compounds that cause high morbidity and mortality; therefore, early initiation of treatment in the emergency department will reduce morbidity and mortality rates (4). The lungs, eyes, skin, and gastrointestinal system are all capable of absorbing OPs well. In terms of how they affect the body, organophosphates stop the enzyme acetylcholinesterase (AChE) from working in synapses in a way that can't be undone. They also make nicotinic and muscarinic cholinergic receptors in the brain, the spinal cord, and the muscles work too hard with acetylcholine (ACh) (5). So, stimulating the muscarinic receptors makes cholinergic symptoms worse, like myosis, bradycardia, nausea, vomiting, abdominal pain, urination, increased bronchial and salivary secretions, and so on. The stimulation of nicotinic receptors makes fasciculations, tachycardia, muscle weakness, and high blood pressure worse. In addition, it causes seizures and loss of consciousness in the central nervous system (6). The diagnosis of OP is based on the identification of the exposure agent, the clinical findings of the patients, and laboratory tests (7). Decontamination, meticulous supportive care, aggressive antimuscarinic therapy (atropine), seizure control, and the administration of oximes are the cornerstones of treatment (5, 7). Niğde is located in the Central Anatolia region of Turkey, while Kars is situated in the Northeastern Anatolia region. The primary areas of focus for development in both cities are agriculture and animal husbandry. The Niğde Ömer Halisdemir University Training and Research Hospital and the Kafkas University Health Practice and Research Hospital (hereinafter referred to as hospitals) are the only tertiary care hospitals and the last referral institutions of the provinces. This study retrospectively analyzed the demographic, clinical and laboratory characteristics of adult patients aged 18 years and older presenting to emergency departments with OP poisoning and to contribute to the management of OP poisoning after the results were obtained.

MATERIAL and METHODS

This study was approved by the Non-Interventional Research Ethics Committee of Kafkas University Application and Research Hospital (Date: 09.11.2023, No: 15). This study was designed as a two-center retrospective study. This study was conducted in accordance with the Declaration of Helsinki (2013 revision). The study was conducted at the Emergency Medicine Clinic of Niğde University Training and Research Hospital and the Emergency Medicine Clinic of Kafkas University Health Practice and Research Hospital. The data of all patients included in the study was recorded in a database set created using Excel. The demographic (age, gender), clinical (exposure agent, route of exposure,

treatment, hospitalization status, length of stay, and mortality status), and laboratory parameters of the patients were analyzed. Hemograms, biochemistry, cardiac markers, blood gases, and coagulation parameters were analyzed using routine blood tests. The levels of pseudocholinesterase requested and detectable in the patients were recorded. The electrocardiography (ECG) was also evaluated, and the findings were categorized as normal, sinus bradycardia, and sinus tachycardia. Findings considered to have an impact on clinical outcomes (length of stay, need for mechanical ventilation, or mortality) in prognosis are reported. Since the study was performed in retrospective design, written informed consent was not obtained from the patients.

Inclusion criteria

The study included patients who applied to the study centers between June 15, 2020, and June 15, 2023, and had an international classification of diseases (ICD) ICD code T60.0 for OP poisoning with a history, clinic, and/or lab confirmation of the diagnosis.

Exclusion criteria

Patients younger than 18 years old, pregnant women, patients whose medical history could not be found or who left the hospital without permission, patients whose file screening was missing information, patients whose ICD diagnosis code was given as OP poisoning but whose diagnosis could not be confirmed by history, clinical, and laboratory findings, and patients known to have a congenital pseudocholinesterase deficiency or non-OP diseases (advanced liver and kidney failure) were not included. In addition, pesticide poisonings not belonging to the OP group were excluded from the study and arrhythmic patients with known bradycardia and basal tachycardia were excluded.

Statistical analysis

In a statistical analysis, the SPSS 22.0 (IBM SPSS Corp., Armonk, New York, USA) package program was used to evaluate the data. In descriptive statistics, categorical data were expressed as numbers and percentages and non-categorical data as mean±standard deviation (SD), or median and interquartile range (IQR). In the comparison of quantitative data, the normality and homogeneity of the variance distribution were checked first. The Shapiro-Wilk and Levene's tests were used for this. The student's t test was used to compare the averages of the data that exhibited a normal distribution; the Mann-Whitney U test or Kruskal-Wallis H test were used for those that did not. In the comparison of continuous variables with each other, Pearson's correlation analysis was used for normally distributed data, and Spearman's rho correlation analysis was used for non-normally distributed data. Since the study had a retrospective design and all patients over 18 years of age (minus exclusion criteria) were included in the study, apriori power analysis was not required. Since retrospective data was used in our study, a voluntary consent form was not required. All data was analyzed at 95% confidence interval (CI) and p<0.05 was considered statistically significant.

RESULTS

A total of 24 patients who met the inclusion and exclusion criteria were included in the study. The median age of the patients was 34 years (IQR, 22.75–58.75). Thirteen (54.2%) of the patients were male, and 11 (45.8%) were female. The most common route of exposure in OP poisonings was oral in 10 patients (41.7%) and inhalation in six patients (25%). The most common form of poisoning was accidental exposure (n=15, 62.5%). All OP poisonings were from the pesticide group, and insecticide poisonings were the most common (n=19, 79.2%). Of the total number of patients in the study, 22 (91.7%) were hospitalized, and only one patient (4.2%) required intubation. The median

Table 1: Baseline characteristics of the patients

Variables	Total n=24
Age, years, median (IQR, 25-75)	34 (22.75- 58.75)
Gender, n (%)	
Male	13 (54.2)
Female	11 (45.8)
Most common exposure route, n (%)	
Oral	10 (41.7)
Nature of poisoning (mostly), n (%)	
Accidental	15 (62.5)
Source of poisoning (mostly), n (%)	
Insecticides	19 (79.2)
Hospitalization, n (%)	
Yes	22 (91.7)
Needing intubation, n (%)	1 (4.2)
GCS score at admission, median (IQR, 25-75)	15 (14-15)
In-hospital mortality, n (%)	
Yes	0 (0)

IQR: Interquartile range, GCS: Glasgow coma scale

Table 2: Organophosphate-related complaints in the patients

Variables	Total n=24
Complaints, n (%)	
Muscaranic	11 (45.8)
Muscaranic + nicotinic	3 (12.5)
Muscaranic + nicotinic + central	7 (29.2)
Muscaranic +central	3 (1.5)
Most common symptoms/findings, n (%)	
Muscaranic	
GIS (nausea, emesis)	21 (87.5)
Nicotinic	
Sinus tachycardia	9 (37.5)
Central	
Confusion	5 (20.8)
ECG findings, n (%)	
Normal	10 (41.7)
Sinus bradycardia	5 (20.8)
Sinus tachycardia	9 (37.5)

ECG: Electrocardiography, GIS: Gastrointestinal system

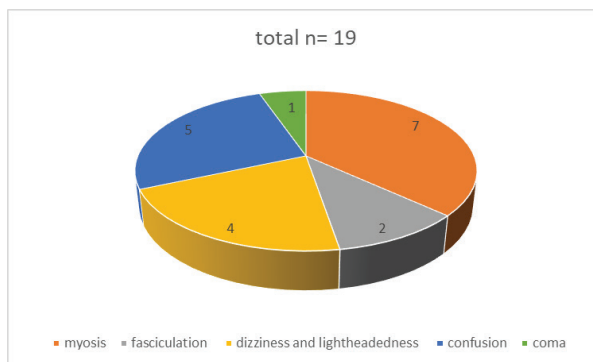


Figure 1. Specific physical examination findings in organophosphate poisoning

value of the Glasgow Coma Scale (GCS) score of patients admitted to hospital emergencies with OP exposure was 15 (14–15). No in-hospital mortality was found. These results are presented in Table 1. The patients' complaints were put into three groups: muscaranic, nicotinic, and central. Eleven patients (45.8%) had only muscaranic complaints, which included those with irritant eye symptoms. Three patients (12.5%) had muscaranic and nicotinic complaints, seven patients (29.2%) had muscaranic and nicotinic and central complaints, and three patients (12.5%) had muscaranic and central complaints. All patients (n=24) had muscaranic-type complaints or findings, with nausea and vomiting being the most common (n=21, 87.5%). Among specific physical examinations, myosis was found in seven patients (29.2%) and fasciculation in two patients (8.3%). Central complaints were observed in a total of 10 patients (41.7%) and included dizziness and lightheadedness in four patients (16.7%), confusion in five patients (20.8%), and coma in one patient (4.2%) (Figure 1). The OP-related complaints of the patients in the emergency department, intensive care unit, and ward follow-up are presented in Table 2. In addition, rhythm analysis revealed normal sinus rhythm in 10 patients (41.7%), sinus tachycardia in nine patients (37.5%), and sinus bradycardia in five patients (20.8%). Table 3 shows the specific treatments that were given to each patient as well as comparisons of their time in the intensive care unit and overall length of stay in the hospital based on their type of intoxication, gender, and ECG rhythm when they were admitted to the emergency room. The median length of stay of patients (n=22, 91.7%) who were hospitalized from the emergency department was 2.5 days (1-3.25), and the median length of stay in the intensive care unit was two days (1.25–3). The pseudocholinesterase levels were studied in a total of 12 patients. In cases of OP poisoning, patients were categorized into two groups: accidental and suicide attempts. In the suicidal group, the mean rank score for the duration of the intensive care stay was higher than in the accidental group (mean rank scores of 7.43 and 5.20, respectively). However, these differences were not statistically significant (p=0.266). In addition, it was found that female patients hospitalized in the intensive care unit were hospitalized for a longer period of time than male patients, but this difference was not statistically significant (mean rank scores of 8.00 and 5.43, respectively; p=0.2). The length of hospitalization was compared according

Table 3: Comparison of ICU length of stay and total length of hospitalization according to gender, type of poisoning and ECG

Variables	Total n=22		p	
Length of hospitalization (time), day, median (IQR, 25-75)				
ICU	2 (1.25-3)			
ICU+ward	2.5 (1-3.25)			
Length of hospitalization (time), day, mean rank				
	Suicide (n=5)	Accidental (n=7)		
ICU	7.43	5.20	0.266*	
ICU+ward	14.61	9.35	0.055*	
	Male (n=11)	Female (n=13)		
ICU	5.43	8.00	0.200*	
ICU+ward	12.50	10.30	0.416*	
ECG at admission in ED, mean rank				
	Normal	Bradycardia	Tachycardia	
ICU	2.00	6.40	7.33	0.352**
ICU+ward	5.55	16.90	13.78	0.003**

Abbreviations: IQR, interquartile range, ICU: Intensive care unit, ECG: electrocardiography, ED: Emergency department, *Mann-Whitney U test; **Kruskal- Wallis H test

Table 4: Correlations between biochemical parameters and clinical outcomes

Correlations		n	r	p*
Total length of hospital	GCS scale	22	-0.714	<0.001
	pH		-0.828	<0.001
	HCO ₃ ⁻		-0.773	0.003
	Anion gap		0.640	0.002
Pseudocholinesterase level	pH	12	0.591	0.043
	HCO ₃ ⁻		0.629	0.028
	Anion gap		-0.688	0.019
	CRP		-0.636	0.026

GCS: Glasgow coma score, HCO₃⁻: Bicarbonate, CRP: c-reactive protein, *: Spearman's rho, n: Sample size, r: Correlation coefficient

to the ECG rhythm (normal, bradycardia, and sinus tachycardia) at the time of presentation to the emergency department; no significant difference was found between the groups in the length of intensive care stay (H(3)=2.086, p=0.352). However, a statistically significant difference was found between the groups in terms of total hospitalization duration rank mean scores (H(3)=11.884, p=0.003). According to the post hoc test (Mann-Whitney U), it was found that this difference between the groups was due to patients with normal ECG; patients with normal sinus rhythm had a shorter hospitalization time than patients with bradycardia and sinus tachycardia (p=0.002 for normal sinus-bradycardia, p=0.006 for normal sinus-sinus tachycardia, and p=0.328 for bradycardia-sinus tachycardia). The mean pseudocholinesterase level was 4934.41±3059.7. In total, 12 patients (50%) were treated with atropine and six patients (25%) with pralidoxime (PAM). A correlation analysis was performed between the continuous variables of the patients using the Spearman's rho test. The total length of hospital stays (n=22)

had a strong negative correlation with GCS, pH, and bicarbonate (HCO₃⁻) (r=-0.714, p<0.001; r=-0.828, p<0.001; r=-0.773, p=0.003, respectively) and a moderate positive correlation with anion gap (r=0.64, p=0.002). In addition, the pseudocholinesterase levels obtained from the patients (n=12) were positively correlated with pH and HCO₃⁻ (r=0.591, p=0.043; r=0.629, p=0.028, respectively) and negatively correlated with anion gap and CRP (r=-0.688, p=0.019; r=-0.636, p=0.026, respectively). These relationships are presented in Table 4.

DISCUSSION

OP poisonings affect both sexes almost equally and are more common in the young population (8). In our study, the male/female ratio was found to be close to each other. Although the rate of males (54.2%) was found to be higher in our study, this difference was not statistically significant (p>0.05). More than half of the patients in our study (n=13) were under the age of 35. In a study by Vucinic et al., they reported that the ratio of

men and women in OP poisonings was approximately equal in terms of gender, similar to our study, but in terms of exposure, the majority were suicide attempts (92%), and the rest were accidental poisonings (9). However, in this study, contrary to what Vucinik et al. reported, we found that the most common poisonings were accidental (62.5%). The main difference between these two situations is that serious poisonings from OP compounds typically result from suicidal oral ingestion in industrialized nations, whereas in developing nations, they typically result from occupational exposure, improper or non-use of protective equipment, or accidental ingestion. Most patients exposed to OP poisoning are usually exposed to these compounds through contact with insecticides and herbicides (10). In our study, insecticides were found to be the most common exposure agent (79.2%). The signs and symptoms of exposure after organophosphate poisoning can be quite wide-ranging. From general gastrointestinal complaints such as mild nausea, vomiting, or diarrhea to severe complaints and findings such as myosis, respiratory distress, bradycardia, fasciculations, seizures, confusion, or coma (11). The Peradeniya Organophosphorus Poisoning (POP) scale developed by Senanayake et al. to evaluate the severity of OP poisoning are used (12). This scale gives each of the five common clinical signs of OP poisoning a score between 0 and 2 points. A seizure is given a score between 0 and 1. The five signs are pupil diameter, respiratory rate, bradycardia, fasciculation, and altered consciousness. Patients are then classified as mild (score 0-3), moderate (score 4-7), or severe (score 8-11). However, due to the retrospective design of this study, a clinical severity scoring could not be performed on patients due to the missing or inadequate recording of the required parameters. Although 91.7% of the patients included in the study was hospitalized for follow-up in accordance with 114 national poison advisory recommendations, only one patient (4.2%) required intubation, and two patients (8.3%) had muscle fasciculation. No in-hospital mortality was found. Since the most common complaints in the study were gastrointestinal such as nausea and vomiting, only one patient needed intubation, two patients with fasciculations, no patients with seizures, and no mortality, the clinical poisoning in patients after OP exposure was not serious. The mechanism of OP intoxication involves phosphorylation of the active serine hydroxyl group. This leads to inactivation of the AChE region, which has an important role in neurotransmission (13). A low erythrocyte AChE or serum AChE level is expected in the confirmation of the diagnosis, but serum pseudocholinesterase is frequently studied for its usability in emergency services. Suppressed pseudocholinesterase activity is a well-known laboratory finding in patients with severe organophosphate poisoning (14). However, the interpretation of AChE and subgroup analysis is still controversial. The levels do not change in proportion with patient clinics; plasma pseudocholinesterase may be found normal or mildly low in emergency room admissions, even in severe poisoning (15-17). In this study, the pseudocholinesterase level was studied in half of the patients (n=12) diagnosed with organophosphate poisoning, and the mean pseudocholinesterase level (4934.41±3059.7) was found to be mildly low (normal range, 5.30–12.90 kU/L). To treat organophosphate or carbamate poisoning, the three main drugs are atropine, glycopyrrolate (GPR), which are anticholinergic drugs, and PAM, which turns

on cholinesterase (18). In this study, atropine was administered as an antidote in 12 symptomatic patients (50%) and PAM in six patients (25%). The atropine was also given to all patients who received PAM. Currently, there is some uncertainty about whether all cases of organophosphate toxicity should receive oxime. This is because some cholinesterase inhibitors bind permanently with cholinesterase after a certain period of time and progress to a process called “aging.” Therefore, PAM should be administered early (first 24-48 hours) and in adequate doses to selected patients (19, 20). We saw that in the clinical setting where PAM was used, the drug was given within the first 48 hours to people who had tachycardia, seizures, changes in consciousness like coma, and muscle fasciculations, in addition to relaxation effects. A study by Ke et al. looked at what factors affect the prognosis of people with OP. They found that the Acute physiology and chronic health evaluation (APACHE)-II score, body temperature, blood pressure, pH, and GCS score were all lower in deceased patients compared to the living; but the creatinine, white blood cell (WBC), alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinin kinase-myocardial band (CK-MB), blood glucose, blood lactic acid, and heart rate were higher in deceased patients (21). In this study, no in-hospital deaths were found. However, low pH, HCO₃⁻; GCS score, and high anion gap were found to be among the factors affecting prolonged intensive care unit hospitalization and total hospital stay. In poisoning, the clinic may be more serious in intentional exposures due to high intakes, the type of substance ingested, the need for specific antidotes, or patient-induced delays in treatment (22). In this study, the mean ranking for the duration of intensive care unit hospitalization, which could indicate clinical severity, was found to be higher in the suicide group. However, this was not found to be statistically significant. There are many studies in the literature examining the effect of gender on intentional exposures (22-24). In a study by Kim et al., there was no discernible difference between genders in terms of the level of intoxication (25). In this study, female patients in the intensive care unit were hospitalized for a longer period of time than male patients but these differences were not statistically significant. However, it was found that patients with sinus tachycardia and sinus bradycardia had longer hospitalizations, and this was statistically significant (p<0.005).

Limitations of the study include the retrospective design leading to data gaps, a small sample size, difficulty in generalizing findings due to data from two small geographic regions, and incomplete parameter records for assessing clinical severity.

CONCLUSION

This retrospective, two-center study sheds light on the demographics, clinical manifestations, and treatment outcomes of adult patients presenting with organophosphate poisoning in emergency departments. The findings emphasize the predominance of accidental exposures, particularly through oral ingestion, and highlight the significance of early intervention in reducing morbidity and mortality rates. The study underscores the importance of assessing clinical parameters, such as GCS, pH, and HCO₃⁻, in predicting the severity and duration of hospitalization. The results contribute valuable insights for informed decision-making in the prevention and management

of organophosphate poisoning. Strategies such as ensuring regular use of personal protective equipment by those working in agriculture and industrial settings, promoting safe farming and industrial practices, implementing measures to restrict access to toxic substances, providing emergency training, conducting public awareness campaigns, and implementing public health measures can be effective in preventing organophosphate poisonings. By adopting these strategies, stakeholders can collaboratively work towards reducing the incidence of organophosphate poisonings and improving overall public health outcomes.

Ethics Committee Approval: This study was approved by Non-Interventional Research Ethics Committee of Kafkas University Application and Research Hospital (Date: 09.11.2023, No: 15).

Informed Consent: Informed consent was obtained from each patients.

Peer Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- A.V., T.D.; Data Acquisition- L.Ş., M.C.A., T.D., A.V.; Data Analysis/Interpretation- A.V., T.D., L.Ş., H.C.; Drafting Manuscript- A.V., T.D., M.C.A.; Critical Revision of Manuscript- H.C., L.Ş.; Final Approval and Accountability- A.V., T.D., L.Ş., M.C.A., H.C.; Supervision- A.V.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

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