

Organophosphorus poisoning: A retrospective study on clinical profile and outcomes in ICU



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ABSTRACT

Background: Organophosphorus (OP) compounds are widely used in India as insecticides and contribute to both acute and chronic poisoning. Several parameters have been analyzed to evaluate the severity of poisoning and to prognosticate the outcome but contradictory results have been obtained from studies for example for the relationship between hypokalemia and outcome, pseudocholinesterase (PChE) levels, and outcome. **Aims and Objectives:** The objectives of this retrospective study were to explore the epidemiological characteristics and clinical profile of patients admitted to intensive care unit with OP poisoning and to evaluate the outcomes including complications, in hospital mortality, and the predictors of mortality. **Materials and Methods:** All the patients above 18 years admitted with a history of ingestion of OP poisoning during the study period were included in the study. Data were collected from case records. **Results:** The mean age of the patients was 34 ± 13.54 . Fifty-four patients were male (69.2%) and 24 were female (30.8%). The correlation coefficient between intubation and PChE levels was 0.266. The mean period of ventilation was $4.16 \text{ days} \pm 2.41 \text{ days}$. About 80% ($n=20$) put on ventilator survived. Correlation of hypokalemia with patients getting ventilator support was 0.26 and that with mortality was 0.038. **Conclusion:** OP poisoning cases were primarily noted in the younger male group with the intent to self-harm. Chlorpyrifos was the most common compound consumed. Early admission and appropriate treatment can reduce mortality and complications as there is no single factor which can be used to predict the outcome in these patients.

Key words: Organophosphorus poisoning; Intensive care unit; Outcomes

INTRODUCTION

Organophosphorus (OP) compounds are widely used in India as insecticides and contribute to both acute and chronic poisoning. It is the culprit in many suicidal poisoning cases reported in the country, especially in rural areas and farming communities. These are easily available as they are components of various insecticides and pesticides and there is no restriction on sale. Early diagnosis and management are important as the mortality rate of up to 30% has been seen even in hospitalized patients.¹

These compounds penetrate the skin and mucosa very well due to the high lipid solubility. They are absorbed rapidly into tissues and cross the blood-brain barrier and affect the central nervous system.^{2,3} OP compounds

inhibit the enzyme acetylcholinesterase which results in the accumulation of acetylcholine in concerned receptors and overstimulation of cholinergic synapses both nicotinic and muscarinic causing various clinical symptoms.⁴ Muscarinic overstimulation causes increased salivation, lacrimation, urination, diarrhea, vomiting, bronchorrhea, constriction of bronchus, and bradycardia while nicotinic overstimulation causes muscle fasciculations, weakness, and diaphragmatic paralysis.⁵ The “intermediate syndrome” or nicotinic syndrome which is characterized by respiratory muscle paralysis including the diaphragm, intercostals, and accessory muscles, cranial neuropathy, proximal limb weakness, and hyporeflexia can occur after 24–96 h after the acute cholinergic syndrome of OP poisoning resolves.^{6,7} About 80% of acetylcholinesterase

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has to be inhibited for failure of nicotinic transmission to occur. This can occur in 8–50% of OP cases. The clinical features point to severity and they are of prognostic importance too.¹

Several parameters have been analyzed to evaluate the severity of poisoning and to prognosticate the outcome but contradictory results have been obtained from studies for example for the relationship between hypokalemia and outcome, pseudocholinesterase (PChE) levels and outcome.⁸⁻¹¹

Aims and objectives

The objectives of this retrospective study were to explore the epidemiological characteristics and clinical profile of patients admitted to the intensive care unit (ICU) with OP poisoning and to evaluate the outcomes including complications, in hospital mortality, and the predictors of mortality.

MATERIALS AND METHODS

We obtained the Institutional Ethical Committee clearance with a waiver of consent (IEC Number: RRMCH-IEC/16/2023). We collected data from patients admitted between January 1, 2018, and December 31, 2022.

Inclusion criteria

All the patients above 18 years admitted with a history of ingestion of OP poisoning during the study period were included in the study.

Exclusion criteria

Patients with concurrent ingestion of another poisonous substance, patients younger than 18 years, and patients whose case records were incomplete excluded from the study.

Data were collected from case records. The collected data included the amount of poison consumed, time interval between ingestion and presentation to hospital and ICU, emergency treatment given, symptoms, coingestion with alcohol, clinical examination findings, investigation results, treatment, ventilator support, tracheostomy, and duration of ICU stay, cause of death – sepsis, cardiovascular, respiratory, and others. Sex, marital status, occupation, route, quantity, manner of ingestion, and time to admission were also collected from the case records. Patient confidentiality was maintained throughout the data collection procedure by the investigators. As electronic data records were not available, data were collected from the original hand-written case sheets stored in the medical records department.

Statistical analysis

The values for continuous variables are expressed as mean and standard deviation; values for categorical variables are expressed as frequency and percentages. Probability values of $P < 0.05$ were considered significant. Correlations were done using Pearson correlation coefficient. R software, R version 4.3.1 (2023) was used for statistical analysis.

RESULTS

We collected data from 78 eligible case files over the period of 5 years.

Figure 1 shows the consort diagram.

The demographic data and clinical characteristics of cases are shown in Table 1.

The mean age of the patients was 34 ± 13.54 . Fifty-four patients were male (69.2%) and 24 were female (30.8%). Age and sex distribution are shown in Figure 2.

Types of poison consumed by patients

Quinalphos-8, dimethoate-10, profenofos-5, chlorpyrifos-17, temephos-3, dichlorvos-11, parathion-5, dichrotophos-5, monocrotophos-5, phenthoate-3, diazinon-3, and other OP compounds-3 were the OP compounds ingested by patients. The most commonly used compound for self-harm was chlorpyrifos and in all cases, the route of consumption was oral. The amount consumed ranged from 5 mL to 200 mL. The mean was 57 ± 47.6 mL. Thirty-five patients consumed < 50 mL, another 35 consumed amounts between 50 and 100 mL and eight patients consumed > 100 mL.

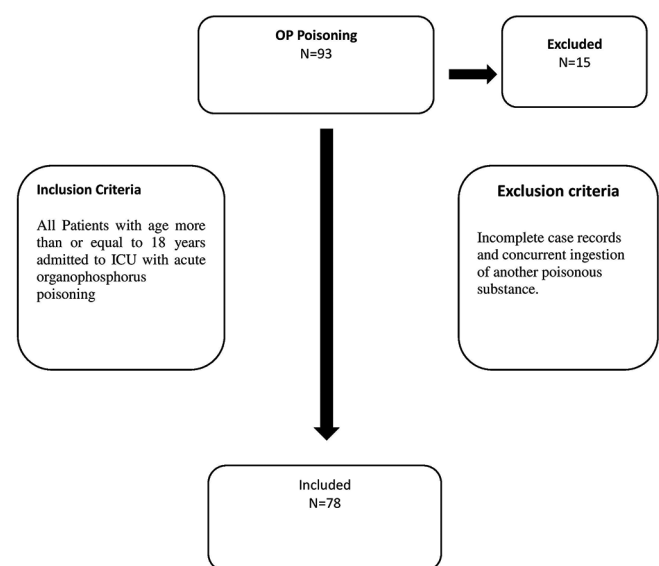


Figure 1: Consort diagram

The time from exposure to the poison and presentation to the hospital was 141 ± 77 min. Out of 78 patients, 34.61% were admitted within 100 min, 51.28% were admitted between 100 and 200 min, and 14.10% patients after 200 min. Out of 78 patients, 18.8% admitted after more than 200 min did not survive while only 3.7% of patients admitted within 100 min expired.

Clinical symptoms and signs on initial admission were sweating (25.64%), vomiting (58.97%), loose stools (15.38%), abdominal pain (21.79%), bradycardia (21.79%), miosis (70.51%), fasciculation (12.8%), bronchospasm (26.92%), tachycardia (11.39%), salivation (20.51%), unconscious (11.53%), and seizures (5.12%).

The initial mean PChE level was 1444 ± 969.02 IU/L. Table 2 shows the relation between initial PChE levels and intubation.

Table 1: The demographic data and clinical characteristics of cases (n=78)

Age (mean±standard deviation)	34±13.54 years
Gender(Male/Female)	69.2%/30.8%
Accidental/Suicidal poisoning	0/100%
Route Oral	100%
GCS at presentation(>8/<8)	79.49%/20.51%
Duration of intensive care unit stay	7.5±5.9 days
Days on ventilator	4.16±2.41 days
Mortality	8.97%

Table 2: Initial pseudocholinesterase levels and intubation

Intubation status	Pseudocholinesterase levels IU/L		
	<700	700–1400	1401–3500
Not intubated	8 (47.06%)	19 (61.29%)	22 (84.62%)
Intubated	9 (52.94%)	12 (38.8%)	4 (15.38%)
Total	17	31	26

P=0.007306

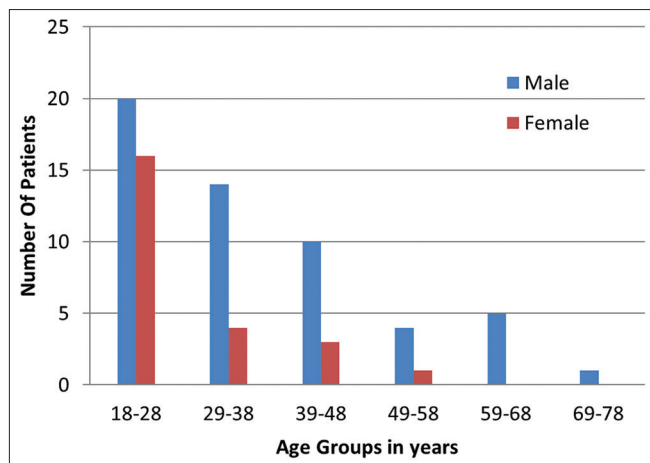


Figure 2: Age and sex distribution

The correlation coefficient between intubation and PChE levels was 0.266. Out of 17 patients who had PChE level <700 IU/L-2 patients expired, in the 700–1400 IU/L range, four expired out of 31 patients and one patient out of 26 patients with PChE level in the 1401–3500 IU/L range expired. P value was found to be 0.186. The correlation coefficient between PChE levels and death was 0.0382.

Hypokalemia was present in 29.48% of patients (n=23). Correlation of hypokalemia with patients getting ventilator support was 0.26 and that with mortality was 0.038. Metabolic acidosis on admission was noted in 8.97% of patients (n=7).

About 32% of patients were intubated, of which 12% of intubations were done on day 2 of admission, and 12% were done on day 4. Therefore, 24% were intubated 24 h after admission. The mean period of ventilation was 4.16 ± 2.41 days. About 80% (n=20) put on ventilator survived. Tracheostomy was done in 5.12% of patients (n=4).

Complications such as sepsis (7.69%), hospital-acquired pneumonia (2.56%), urinary tract infection (3.8%), thrombophlebitis (5.12%), diabetic ketoacidosis (1.28%), and neuroencephalopathy (1.28%) were found in the patients.

Out of the 78 patients, 6.4% of patients were known cases of diabetes mellitus, 5.12% were hypertensive, and 1.28% was known chronic obstructive pulmonary disease.

DISCUSSION

In this retrospective study, 78 patients were identified with OP poisoning and the mortality rate in the ICU was calculated to be 8.9%. The time gap between emergency hospital care and intake of poison will always affect the outcome. The more the lag time from consumption of poison to admission the chance of survival is reduced. As our hospital is located close to a highway in a rural area, the accessibility to patients would have been easier.

The previous studies have shown that the incidence of poisoning is more in males compared to females. The mean age group was 34 ± 3 similar to other studies.¹ Younger males succumb to the pressures and conflicts of life and bear the burden of the family.

Psychiatric illness¹² including depression is commonly seen in patients as most of the poisoning cases are suicidal in nature. In this study, out of the 78 case records, 100% of cases were found to be suicidal attempts or with intent to

self-harm. Psychiatry consultation and counseling were given to all patients and psychiatric follow-up was advised on an individual basis

Management of acute OP poisoning consists of supportive therapy, a muscarinic antagonist commonly atropine, and an acetylcholinesterase reactivator like oxime that reactivates acetylcholinesterase.^{5,13} Atropine is a muscarinic acetylcholine receptor antagonist. OP compounds form a phosphorylated enzyme with acetylcholinesterase. The enzyme reactivates spontaneously by a slow process which can be facilitated and fastened by reactivators like oximes. The ageing reaction which occurs 48–72 h after the poisoning can hamper this activation. Different OP compounds have different ageing half-lives. OP compounds such as parathion and chlorpyrifos form diethylphosphorylated acetylcholinesterase which has a long aging half-life while the ageing half-life of dimethylphosphorylated acetylcholinesterase formed by agents such as malathion, dimethoate, and oxydemeton is very short. When the ageing half-life is short, reactivation by oximes cannot occur over a long time periods.⁷ Oximes may or may not be beneficial as there is inconclusive evidence.^{5,14-16} Oximes are recommended to be used in symptomatic patients. Randomized trials are few in this area; therefore, ideal treatment regimens are not available.¹³ All patients were managed according to standard treatment guidelines, gastric lavage and skin decontamination were done and treated with atropine and oximes according to requirement and clinical features. All patients received atropine and pralidoxime in this study. All patients received supportive care in the ICU depending on the clinical scenario. Antibiotics were administered to treat as well as to prevent infections. Intubated patients were given care according to ventilator-associated pneumonia care bundle. Nutrition and physiotherapy were all done on an individual basis for all patients.

The normal PChE levels reference used in our biochemistry lab is as follows, males: 4620–11500 IU/L and in females 3939–10800 IU/L. Kumar et al. defined the severity of poisoning according to the serum PChE levels, with latent being a pseudocholinesterase level >50% of normal. Mild, moderate, and severe were pseudocholinesterase level 20–50% of normal value, 10–20% of normal, and <10% of normal (<700 IU/L), respectively.^{17,22}

The severity of acute OP poisoning correlates with the decrease in pseudocholinesterase activity.¹⁸⁻²⁰ While some studies have shown that a low level of the enzyme does not indicate the severity of the poisoning.¹⁰ We recorded the initial PChE levels from the case sheets. Some patients

serial monitoring of PChE were not done therefore data were not available. The PChE levels were decreased in 94.9% of the cases on the initial day of presentation. About 42% of patients had PChE levels <1000 IU/L and 57.69% had PChE more than 1000 IU/L. More than 50% of patients presenting with severe poisoning were intubated. More intubations occurred in the severe and moderate cases compared to mild cases. The correlation coefficient between intubation and PChE levels was 0.266 which is not negligible. The correlation coefficient between PChE levels and death was 0.0382 which is very small.

Studies have shown that hypokalemia can increase morbidity and mortality in OP poisoning cases.^{8,9} Hypokalemia is a common finding in OP poisoning but the exact reason is not known. Hypokalemia-induced muscle weakness can contribute to the respiratory paralysis caused by the poison. It can also cause arrhythmias contributing to morbidity and mortality. About 29% of patients were found to have hypokalemia in this study. Evaluation was done and it was treated with potassium supplementation orally or intravenously. Correlation between hypokalemia and mortality was found to be weak. The previous studies have shown a positive correlation between mortality, morbidity, and hypokalemia.^{8,9}

The majority of the patient population is from rural farming areas. OP compounds therefore are easily available in these areas. The quantity of poison ingested was noted but this cannot be always relied on because the information might not be always accurate, it could be assumed from the amount left in the bottle and the patient might not be oriented enough to give a proper history. For patients brought in unconscious and in altered sensorium, history might be heavily unreliable.²¹ In some cases, information of poison consumed was given by caregivers hours after the patient was admitted. The kind of OP compound ingested determines the outcome and severity.²³

There were two cases of documented intermediate syndrome among the 78 case records reviewed. Incidence of intermediate syndrome has not been associated with any specific compound.^{24,25} The exact etiology and pathophysiology are unclear and the best treatment modality is supportive care.

Limitations of the study

Our study is a retrospective study based on case records. All cases of OP poisoning during the time could not be studied as there were missing data in the case records.

CONCLUSION

OP poisoning cases were primarily noted in the younger male group with the intent to self-harm. Chlorpyrifos were the most common compound consumed. Early admission and appropriate treatment can reduce mortality and complications as there is no single factor which can be used to predict the outcome in these patients.

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