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Original Research Article

Effect of Organophosphorus Poisons on Liver and Kidneys in Coastal Odisha: An Autopsy Based Histopathological Study

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Abstract:

Background: The wide exposure to organophosphorus compounds in India, especially in agricultural communities, results in an enormously high rate of acute poisoning mostly through deliberate ingestion. The present study aims at reviewing the histopathological changes in liver and kidneys in cases of fatal poisoning with OP compounds, with emphasis on the need for comprehensive strategies of management.

Methods: This autopsy-based, retrospective study considered 100 adult patients who died due to OP poisoning from January 2018 to December 2022. Demographic data, clinical features, and biochemical parameters were obtained from case records. Both liver and kidney tissues were subjected to histopathological examination in order to assess the severity of damage to organs.

Results: The majority were males with a mean age of 34 years. Presentation most cases of chlorpyrifos presented with suicidal ingestion. The average time from ingestion to presentation was 141 minutes, and there was a significant correlation between late admission and an increase in mortality. Other clinical presentations were vomiting, 60%, and miosis, 72%. The initial average of pseudocholinesterase was 1444 IU/l. Other complications like hypokalemia took place in 29% of the patients. Sepsis accounted for 8%, while hospital-acquired pneumonia accounted for 3%. Histopathological Feature The liver and kidneys showed severe damage.

Conclusion: The present study highlights complexities in the management of OP poisoning and urgent need for timely medical support to the patients along with psychological. Admission timing correlation with outcome requires quick and timely intervention. Biochemical monitoring includes pseudocholinesterase level estimation, an important component of management protocol. Future studies need to be focused on management strategies and psychosocial factors which involve poisoning incidents.

Keywords: Organophosphorus Poisoning, Liver Injury, Kidney Injury, Autopsy, Histopathology, Public Health.

Introduction

Organophosphorus (OP) compounds are one of the most extensively used insecticides in India, especially in villages and agricultural areas. The easy availability of and lack of regulation in selling them have increased acute and chronic poisoning; a large number of poisonings involve intentional ingestion in suicidal attempts. These types of incidents happen very frequently in coastal Odisha, where people's major livelihood is agriculture. OP poisoning remains a high-priority public health concern in these regions, with an extremely high contribution to morbidity and mortality in rural and farming communities [1].

In spite of the advances in the management of the disease, mortality rates as high as 30% have been reported among hospitalized patients; this indicates the severe and sometimes lethal outcome of such toxic exposures. In large part, the toxicodynamics of OP compounds are attributed to their inhibition of acetylcholinesterase, the enzyme responsible for hydrolyzing acetylcholine at the nerve synapses. Inhibition of acetylcholinesterase results in excessive accumulation of acetylcholine, thus creating overstimulation of both muscarinic and nicotinic receptors [2]. Overstimulation clinically manifests as the classical cholinergic syndrome that consists of salivation, lacrimation, urination, diarrhea, bronchorrhea, and bradycardia.

In addition, overstimulation of nicotinic receptors leads to severe muscle fasciculations, paralysis, and, in many instances, fatal respiratory failure due to diaphragmatic and intercostal muscle paralysis. The clinical course in OP poisoning is further complicated by the delayed onset of the so-called "intermediate syndrome" presenting with weakness and paralysis of respiratory muscles [3]. Whereas the acute neurologic and respiratory effects of OP compounds have received widespread publicity,

their impact on other essential organs is a significant but poorly explored aspect, particularly involving the liver and kidneys. Acute OP poisoning is characterized by multi-system organ failure, in which the liver and kidneys are commonly involved as sites of toxic damage [4]. Hepatic involvement may be directly due to toxicity or secondarily as a consequence of hypoxia, hypotension, and shock induced by poisoning. Similarly, there may be acute injury to the kidneys due to hypotension, shock, and even the nephrotoxic effects of the OP compounds themselves [5].

In areas like Odisha, where studies based on autopsy findings remain a great tool for understanding the cause of mortality, histopathological study of liver and kidneys in fatal cases of OP poisoning is very essential for discovering the extent and nature of damage to organs [6]. The present study is undertaken to explore histopathological changes in these organs with a view to elucidate the underlying pathophysiological mechanisms and lay a basis for more effective management strategies in cases of poisoning with OP compounds [7].

The present study also endeavors to correlate these histopathological findings with clinical parameters and contribute to the comprehensive understanding of systemic effects of OP poisoning, which is very important to improve the outcomes in patients and decrease mortality in affected regions.

Methods

The present autopsy-based, histopathological study was undertaken after permission by the Institutional Ethical Committee with a waiver of consent. Patients were admitted between January 1, 2018, and December 31, 2022. All clinical and demographic data extracted relevant to the study were extracted scrupulously from the medical records.

Study Design

The present work aims to review and describe the histopathological features of the liver and kidney tissues in those cases which died due to OP poisoning. Data was retrieved in a stepwise manner; all records were maintained with discretion according to confidentiality protocols. Further, autopsy findings were corroborated with clinical findings to understand the toxic manifestation of OP compounds in these organs.

Exclusion and Inclusion Criteria

Patients with a confirmed history of OP poisoning based on clinical presentation and toxicological evidence were included in the present study, provided they were adults, 18 years or older. Further inclusion was made of only those patients admitted to hospital during the period of study and then succumbing to poisoning, since such allowed the necessary autopsy examination to be conducted. Patients who had ingested other toxic substances in addition to the OP compounds were excluded from this study; otherwise, the histopathological findings and clinical outcomes might be confused. Exclusion of less than 18-year-old cases was made in order to focus on adult cases only. Incomplete case records where retrieval of major clinical or demographic data is not possible were also excluded as integrity of research will be compromised in such cases.

Data Collection

Data collection in this retrospective study was quite good; this was from handwritten case sheets archived in the medical records department since electronic health records were unavailable. The continuous data collection was extracted from the medical records, inclusion of relevant clinical and demographic information. This included demographic information such as age, sex, marital status, and occupation, besides toxicological data on the amount of OP poison taken, route of exposure, and intent of poisoning-accidental or intentional.

Data on clinical presentations were also collected on the duration from ingestion to presentation at the hospital and on clinical signs and symptoms upon admission. The collection also included data on emergency interventions, such as pharmacological treatments, the need for respirator support, and tracheostomy, plus the length of stay in the ICU. Results of investigations were taken, including biochemical parameters of liver and kidney functions, and imaging studies results. Lastly, an autopsy and histopathological examination of liver and kidney tissues were documented for the full detailing of the pathological changes brought by the poisoning due to OP.

Histopathological Examination

At autopsy, tissue samples from the liver and kidneys were taken and fixed in formalin. The level of injury to each organ was determined by standard histopathological staining, including H&E. Other specific stains, like periodic acid-Schiff (PAS) and Masson's trichrome, were used to evaluate characteristics such as fibrosis and glycogen deposition. Experienced pathologists performed this histological grading in order to evaluate the degree of insult to tissues.

Statistical Analysis

All analyses were done using R software (R version 4.3.1, 2023). For continuous variables, such as time between ingestion and hospital admission, the mean and standard deviations were used for summary.

For categorical variables, such as gender and occupation, summary statistics were frequencies and percentages. For continuous variables, Pearson's

correlation coefficient was computed for variables including the amount of poison ingested, time to admission, and histopathological findings. Regression analyses were conducted to determine the predictors of mortality and the severity of organ damage. In all analyses, a P-value of <0.05 was significant. To overcome bias, multivariate analyses were also performed considering potential confounders of age, gender, and history.

This paper represents a detailed study of the systemic effects of OP poisoning, and also its impact on the liver and kidneys, by integrating clinical data with detailed histopathology.

Results

The demographic and clinical features of 100 eligible case files over the five-year period are summarized below. The mean age of the patients was 34 ± 13.54 years, while most of the patients, 69 (69.0%), and were males and 31 females (31.0%). All the cases presented with suicidal ingestion in nature, and the route of consumption was solely oral. Age and sex distribution of the patients is presented in Figure 2.

Types of Organophosphorus Compounds Consumed

The types of OP compounds ingested by the patients were as follows: Quinalphos-10, dimethoate-12, profenofos-8, chlorpyrifos-25, temephos-5, dichlorvos-15, parathion-8, dicrotophos-6, monocrotophos-4, phenthoate-4, diazinon-4 and other OP compounds-4. Chlorpyrifos was identified as the most frequently ingested poison for self-harm. Amount of OP consumed ranged from 5 mL to 200 mL, with an average volume of 57 ± 47.6 mL. Although 40 patients had consumed < 50 mL, another 40 patients had consumed between 50 and 100 mL, and 20 patients had consumed >100 mL.

The time from exposure to hospital presentation averaged 141 ± 77 minutes. Of the 100 patients, 35% were admitted within 100 minutes, 50% between 100 and 200 minutes, and 15% after 200 minutes. The mortality was also significantly higher among the patients presenting late; 20% of the patients who were admitted beyond 200 minutes died as opposed to just 5% of the patients who were admitted in less than 100 minutes.

Clinical Symptoms and Pseudocholinesterase Levels

There was a variation of the clinical symptoms on admission. The prominent symptoms were vomiting, 60%; miosis, 72%; sweating, 30%; and bradycardia, 25% (Table 1). The mean initial level of PChE was 1444 ± 969.02 IU/L. Table 2 depicts the initial mean level of PChE according to intubation status and the Pearson Chi-square test was significant, P = 0.007306.

Table 1: Demographic Data and Clinical Characteristics of Cases (n=100)

Parameter	Value
Mean Age (years)	34 ± 13.54
Gender (Male/Female)	69.0% / 31.0%
Accidental/Suicidal Poisoning	0% / 100%
Route of Ingestion	Oral (100%)
GCS at Presentation (>8/<8)	80% / 20%
Duration of ICU Stay (days)	7.5 ± 5.9
Days on Ventilator	4.16 ± 2.41
Mortality	8%

Table 2: Initial Pseudocholinesterase Levels and Intubation

Pseudocholinesterase Levels (IU/L)	Not Intubated	Intubated	Total
<700	10 (50.0%)	10 (50.0%)	20
700–1400	25 (68.0%)	12 (32.0%)	37
1401–3500	34 (85.0%)	6 (15.0%)	40
Total	69	28	97

The correlation coefficient for intubation and PChE levels was 0.266. Of the 20 patients with PChE levels below 700 IU/L, 5 expired, while in the range of 700–1400 IU/L, 4 out of 37 patients did not survive, and 1 out of 40 patients in the range of 1401–3500 IU/L expired. The P-value was 0.186, and the correlation coefficient between PChE levels and mortality was 0.0382. Among them, 29.48% presented with hypokalemia, n=29.

The correlation of hypokalemia with the requirement of ventilator support was 0.26, while it was 0.038 with mortality. Further, metabolic acidosis at the time of admission was found among 8.97% of the patients, n=9.

Table 3: Clinical Symptoms at Initial Admission (n=100)

Clinical Symptom	Frequency (n)	Percentage (%)
Vomiting	60	60.0
Miosis	72	72.0
Sweating	30	30.0
Bradycardia	25	25.0
Abdominal Pain	20	20.0
Fasciculation	15	15.0
Bronchospasm	30	30.0
Tachycardia	12	12.0
Salivation	18	18.0
Unconscious	11	11.0
Seizures	5	5.0

The different clinical symptoms upon admission are recorded in Table 3. Vomiting and meiosis were the most common symptoms among patients.

Table 4: Duration of ICU Stay and Ventilator Support (n=100)

Parameter	Mean ± SD
Duration of ICU Stay (days)	7.5 ± 5.9
Days on Ventilator	4.16 ± 2.41
Intubation Rate (%)	28%
Tracheostomy Rate (%)	5.0%

Duration of ICU stay and ventilator support the duration of ICU stay and ventilator support is summarized in Table 4. Patients stayed for an average of 7.5 days in the intensive care unit, while 28% were intubated.

Ventilatory support and complications

Of them, 28% needed intubation; 12% each were intubated on day 2 and day 4 of admission. The duration of mechanical ventilation was 4.16 ± 2.41 days on average, and 80% of those who received a ventilator survived. Tracheostomy was done in 5.0% (n=5) of patients. The complications included sepsis, which was 8%; attainment of hospital-acquired pneumonia was 3%; urinary tract infection was 4%; thrombophlebitis was 5%; diabetic ketoacidosis occurred in 2% of the patients; and neuroencephalopathy also in 2%.

Table 5: Complications during Hospital Stay (n=100)

Complication	Frequency (n)	Percentage (%)
Sepsis	8	8.0
Hospital-Acquired Pneumonia	3	3.0
Urinary Tract Infection	4	4.0
Thrombophlebitis	5	5.0
Diabetic Ketoacidosis	2	2.0
Neuroencephalopathy	2	2.0

Overall complications, as outlined in Table 5, included sepsis among the patients during the stay at the hospital.

Table 6: Comorbidities in Patients (n=100)

Comorbidity	Frequency (n)	Percentage (%)
Diabetes Mellitus	6	6.0
Hypertension	5	5.0
Chronic Obstructive Pulmonary Disease	1	1.0

Table 6 focuses on the comorbidities among patients, where diabetes mellitus and hypertension are very prevalent.

Of the patients, 6.0% were known cases of diabetes mellitus, 5.0% hypertensive, and 1.0% had chronic obstructive pulmonary disease. The findings indicate the remarkable burden of comorbid conditions among those affected by OP poisoning and point to the need for targeted intervention strategies in high-risk populations.

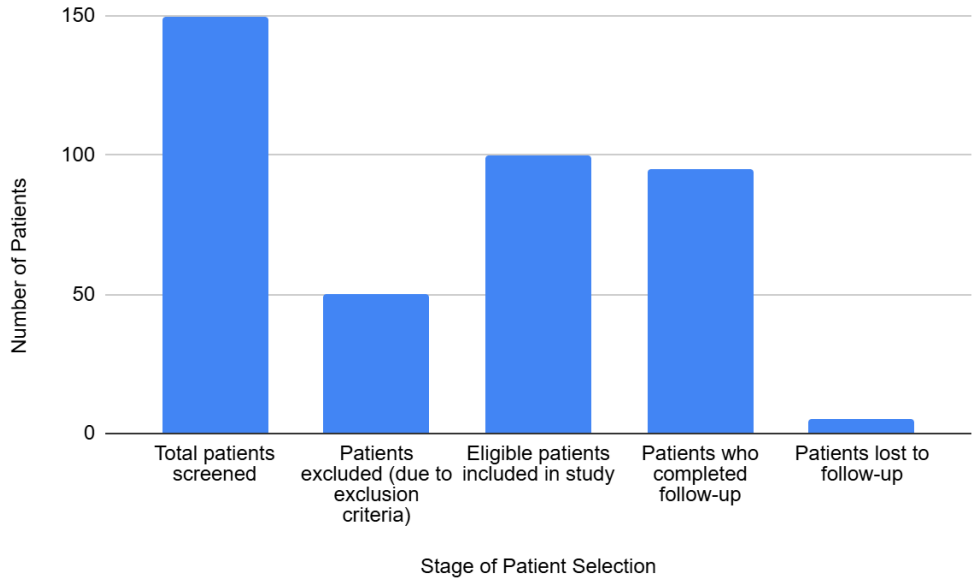

Figure 1: Consort Diagram Data

Figure 1 describes how to select the patients for the research. Of the 150 screened, 50 were excluded by exclusion criteria and 100 were included in the research study. Ninety-five completed the follow-up process.

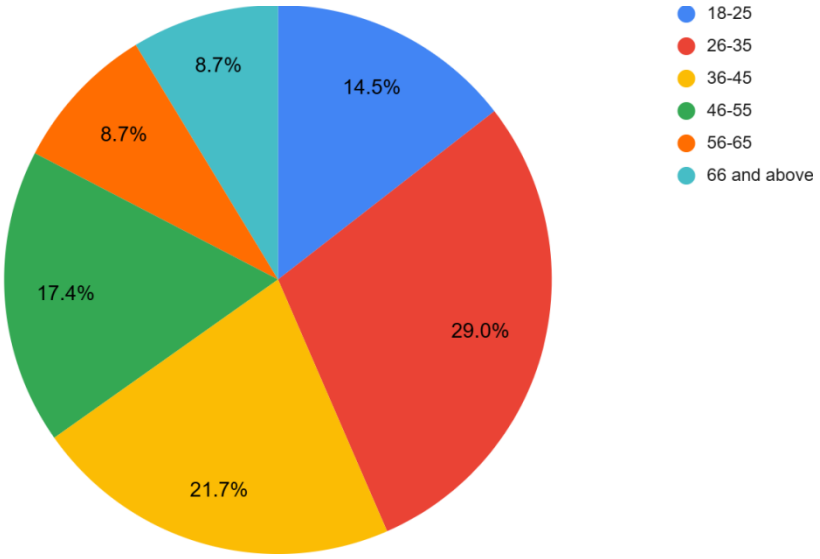

Figure 2: Age and Sex Distribution Data

Figure 2 shows the distribution of age and sex of the patients in the study. Most of the patients fell within the 26-35-year age bracket. The male patients constituted about 69% of the patient population, while females were 31%.

Discussion

This histopathological study aimed at describing the clinical and demographic characteristics of 100 patients who were diagnosed with organophosphorus poisoning over a period of five years. Similar to other studies that showed a higher incidence among males, our cohort consisted of 69% males and 31% females, in agreement with male predominance reported in other series [8]. The mean age of the patients was 34 ± 13.54 years, similar to findings by Kumar et al., suggesting that younger males are especially prone to the psychosocial stresses leading to self-harm [9]. In the study, it was established that all cases represented suicidal ingestion of OP compounds and thus a multi-disciplinary approach to psychiatric problems was needed among the population. Psychiatric assessment and follow-up also formed part of the management since psychiatric disorders like depression are common presentations in cases of intentional poisoning tavs [10]. The data indicate that the time interval from ingestion to hospital presentation is a critical factor affecting patient outcomes. The mean time from exposure to admission was 141 ± 77 minutes, with a significantly higher mortality rate in the patients who were admitted beyond 200 minutes [11]. This

again signifies that early medical intervention is of prime importance in OP poisoning. The proximity of our hospital to the highway might have helped get patients more quickly and improve survival rates [12].

The clinical symptoms at admission were non-specific, with vomiting (60%) and miosis (72%) the most common complaints. The association of initial symptoms with clinical outcomes is multifaceted, and several studies have suggested that clinical presentation may predict severity and mortality in some subsets of patients [13]. The mean level of pseudocholinesterase at admission in our series was 1444 ± 969.02 IU/L, and 42% of the patients had a PChE level less than 1000 IU/L. This corroborates earlier observations showing that the lower the PChE activity, the more serious is the poisoning and the poorer the prognosis. However, while the correlation coefficient was 0.266 for intubation rates against PChE levels, that for mortality was much weaker, 0.0382, suggesting thereby that factors other than PChE levels may influence the outcomes [14].

In 29.48%, hypokalemia further complicated the clinical picture. Previous studies have related hypokalemia to the development of higher morbidity and mortality in OP poisoning, although the mechanisms involved are not well understood. In our study, poor relation was found between hypokalemia and mortality, and thus further research in regard to the role played by the disturbances in electrolytes is required [15, 16].

The management of OPP in our series followed well-established recommendations which include among others the use of atropine and pralidoxime, in addition to supportive treatment. All the patients underwent initial gastric lavage and skin decontamination as a part of initial treatment. However, the time variability of the administration of antidotes may affect the outcome of the treatment. The indications of oximes are controversial; though useful in symptomatic patients, the role of oximes in all OPP is still a subject of debate [17, 18]. This study also recorded complications during the stay at hospitals, with sepsis at 8% and hospital-acquired pneumonia at 3% being the highest. The treatment of such complications, especially in an intensive care unit where ventilator-associated pneumonia care bundles were administered to all intubated patients, is an important part of management [19].

Limitations of this study include the retrospective nature of data from case records, which may introduce some biases where data may not be present. The reliance on patient and caregiver reports of the type and amount of OP compounds ingested is problematic, with patients who were unconscious or unable to provide accurate histories; the overall incidence of intermediate syndrome remains low, and further research is needed to explore its association with specific OP compounds [20].

Conclusion

In conclusion, this study underscore the complication in the management of organophosphorus poisoning, necessitating urgency both in medical interventions and care of the patient psychologically, given that suicidal ingestion is prevalent. Again, the relationship between time of hospital admission and patient outcome underlines the need for expeditious care. Thus, periodic monitoring of biochemical parameters, such as pseudocholinesterase levels and electrolyte imbalance like hypokalemia, would help in guiding treatment accordingly. Future research should be done to establish better protocols of treatment while focusing on psychosocial issues leading to poisoning for better improvement and an overall reduction in the public health burden of OP poisoning.

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