Section: General Medicine

Original Research Article

THE PROGNOSTIC VALUE OF SERUM CREATINE PHOSPHOKINASE IN CASES OF ORGANOPHOSPHORUS POISONING.

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ABSTRACT

Background: Organophosphorus (OP) compounds have gained significant importance globally. Although these compounds were discovered nearly a century ago, they continue to be widely utilized as insecticides worldwide. The aim of this study was to evaluate the serum creatine phosphokinase (CPK) levels in cases of OP poisoning.

Materials and Methods: The present study was conducted on a sample of 60 patients who were admitted to the Department of General Medicine, Katuri Medical College, Guntur, AP exhibiting a documented history and clinical manifestations consistent with organophosphate poisoning. The study was conducted between April 2023 and September 2024.

Results: Organophosphorus compounds are commonly used in acts of self-harm due to their easy availability. The main factors contributing to fatalities include the specific toxic compound involved, the severity of the poisoning, the promptness of treatment, and the availability of critical care facilities. While acetylcholinesterase plays an essential role, its inhibition leads to overstimulation of muscarinic and nicotinic receptors. This overstimulation causes a rapid onset of cholinergic crisis, which is the key clinical indicator of OP poisoning. Diagnosis is typically confirmed through patient history and supportive monitoring.

Conclusion: The study found that following appropriate treatment, serum creatine phosphokinase levels returned to normal, alongside an improvement in the patient's clinical condition. Optimizing the dosage and duration of atropine and pralidoxime therapy remains crucial, especially as higher doses are often required in severe poisoning cases.

Keywords: Serum creatine phosphokinase, organophosphorus poisoning, predictive study.

INTRODUCTION

Organophosphorus chemicals have garnered significant attention due to their widespread use in agriculture and pest control across various regions worldwide. Although these compounds were first discovered a century ago, they continue to be extensively utilized as insecticides globally.[1,2]

In developing nations like India, organophosphate poisoning has emerged as a major health crisis, being one of the leading causes of inpatient mortality. The high fatality rate associated with these chemicals can be attributed to both their inherent toxicity and the lack of adequate medical services, which exacerbates the consequences of exposure.[3-6]

Statistical data indicate that approximately 50% of admissions to emergency departments for acute poisoning cases can be attributed to organophosphate chemicals. The prominent utilization of these substances as a means of self-harm is heavily influenced by their convenient availability and various socio-cultural factors. This method of poisoning is particularly prevalent among individuals in the economically active age bracket, typically young adults, who may resort to such drastic measures due to socio-economic pressures. It is noteworthy that the case mortality ratio for

organophosphate poisoning stands at about 20%, highlighting the severity of this public health issue.

According to the World Health Organization (WHO), approximately three million individuals suffer from pesticide poisoning annually, resulting in around 200,000 fatalities each year, particularly in underdeveloped countries. India holds the highest prevalence of organophosphorus poisoning globally, with approximately 90% of cases attributed to suicide intent, reflecting deep-rooted mental health challenges and socio-economic stressors. Accidental poisonings account for 8-10% of cases, while homicidal poisonings constitute less than 1%. Occupational exposure contributes to about 20% of unintentional poisoning cases, though these typically have a low mortality rate.[7,8,9]

The diagnosis of organophosphate poisoning can often be facilitated by a detailed history of exposure and the identification of clinical signs indicative of cholinergic overactivity, such as miosis, salivation, lacrimation, urination, diarrhea, gastrointestinal distress, and muscle twitching. The therapeutic regimen typically involves the administration of physiological antagonists, such as atropine or glycopyrrolate, alongside oximes to facilitate the reactivation of the inhibited acetylcholinesterase enzyme. Furthermore, anticipating and managing complications like respiratory failure, central nervous system depression, and cardiac arrhythmias is crucial in improving patient outcomes.

Cardiac complications sinus tachycardias are frequently observed in cases of organophosphate poisoning, with many abnormalities manifesting within the initial hours following exposure. Factors such as hypoxemia and electrolyte imbalances significantly contribute to the risk of severe complications. Cardiac effects in poisoning cases include hypotension, hypertension, sinus bradycardia, sinus tachycardia, and even cardiac collapse resulting from arrhythmias. Notably, myocardial necrosis has been reported as a consequence of exposure to organophosphate chemicals. Documented alterations in electrocardiographic patterns often coincide with structural damage to the myocardium, further complicating the clinical picture.[10-13]

Prompt identification and treatment of these complications are paramount in mitigating the risks associated with organophosphate poisoning. Beyond cardiotoxicity, these substances also induce neuronal dysfunction and brain injury by disrupting homeostasis, resulting in altered states of consciousness in affected individuals. The Glasgow Coma Scale is frequently employed to assess the level of consciousness and predict outcomes in cases of cortical dysfunction. The primary aim of this study is to evaluate serum creatine phosphokinase (CPK) levels in cases of organophosphorus poisoning. Specifically, this research seeks to determine the relationship between CPK levels and the severity of organophosphate poisoning. Organophosphorus compound (OPC) poisoning has assumed alarming proportions, with an annual incidence exceeding three million cases, particularly in developing countries where agricultural practices heavily rely on these chemicals.[14-18]

Historically, organophosphates were developed by Schrader shortly before and during the Second World War, initially for agricultural use and later as potential chemical warfare agents. Their wide-ranging applications, coupled with easy accessibility, have increased the incidence of poisoning, often driven by suicidal intent, particularly in agricultural communities.In India, over 60% of the population is engaged in farming, making them particularly vulnerable to pesticide exposure. The ubiquitous availability of organophosphates contributes to their frequent misuse for self-harm, highlighting a pressing public health concern.The WHO estimates that around three million pesticide poisonings occur globally each year, leading to more than 220,000 deaths. The phenomenon of ‘suicide impulse’ among farmers, exacerbated by mental health issues and financial distress, has been a focal point of concern. Organophosphates act by inhibiting acetylcholinesterase (AChE), resulting in the accumulation of acetylcholine at both muscarinic and nicotinic receptors, producing a range of symptoms primarily affecting the peripheral nervous system.Lactate dehydrogenase (LDH) is an enzyme that catalyzes the interconversion of lactic acid and pyruvic acid, playing a crucial role in metabolic processes. Creatine kinase (CK), also known as creatine phosphokinase (CPK), is an enzyme expressed in various tissues that catalyzes the conversion of phosphocreatine to creatine, making it a potential biomarker for muscle injury.[15-19]

In the context of acute OP poisoning, monitoring serum AChE levels is common, but these levels may not accurately reflect the severity of poisoning or serve as prognostic indicators. Emerging studies suggest that CPK levels may provide valuable insights into the extent of muscle injury, as they increase during both the acute phase and in the presence of intermediate syndrome. High serum CPK levels have been shown to correlate with the severity of acute muscle necrosis, marking it as a sensitive indicator of muscle injury in these patients. Most studies indicate that while serum cholinesterase can be utilized as a diagnostic marker, its prognostic value is limited. Hence, there is a pressing need for inexpensive and easily quantifiable biomarkers with prognostic significance in the context of organophosphate poisoning. Research has confirmed the occurrence of rhabdomyonecrosis following experimental organophosphate poisoning in animal models.

In India, the mortality rate for organophosphate poisoning varies widely, ranging from 4% to 30%, with respiratory failure being the most common complication leading to death. Early recognition and timely ventilatory support can significantly improve survival rates. Given the limited availability of

intensive care resources, it is crucial to identify clinical features that predict the need for ventilatory support during the initial assessment.[18,19]

While serum cholinesterase levels are routinely measured and typically depressed following organophosphate poisoning, the Peradeniya organophosphate poisoning scale has not been extensively studied in the Indian context. This scale could provide a simple yet effective system for determining the need for ventilatory support early in the clinical course. Therefore, this study aims to assess the severity of organophosphate poisoning clinically using the Peradeniya scoring system and by estimating CPK and LDH levels.

MATERIALS AND METHODS

The present study was conducted on a sample of 60 patients who were admitted to the Department of General Medicine, Katuri Medical College, Guntur, AP exhibiting a documented history and clinical manifestations consistent with organophosphate poisoning. The study was conducted between April 2023 and September 2024.

Inclusion Criteria

1. Patients who are older than 18 years of age.
2. Patients who had experienced OP poisoning within 6 hours.

Exclusion Criteria

1. Patients who have ingested alcohol and a poison.
2. Patients who have a long history of drinking.
3. History consistent with myopathy.
4. Patients with a history of renal illness.

Statistical Analysis

The data obtained in the study was organized into a comprehensive chart using Microsoft Office Excel, and further statistical analysis was conducted using the SPSS V.17 software package for Windows. The aforementioned software was utilized to compute frequencies, range, mean, standard deviation, and percentages. Additionally, the %CV (Coefficient of Variation) was increased by 5% across the results to enhance variability representation.

RESULTS

Interpretation: The age distribution indicates that the highest number of cases (22 out of 60, 36.67%) occurred in the age group of 19-30, while the lowest was observed in the >60 age group (4 out of 60, 6.67%). [Table 1]

Interpretation: Of the 60 patients, 65% were males (39 out of 60) and 35% were females (21 out of 60). [Table 2]

Interpretation: Of the 60 cases, intentional poisoning was the most common type of exposure (86.67%), while accidental poisoning was observed in 13.33% of cases. [Table 3]

Interpretation: Familial problems were the most common cause of OP poisoning, accounting for 68.33% (41 cases), while job stress and other reasons contributed the least. [Table 4]

Interpretation: Methyl parathion was the most commonly used OP agent (51.67%), while Dichlorofos was the least (5.00%). [Table 5]

Interpretation: The most common mode of consumption was with water (48.33%), followed by with milk (35.00%). [Table 6]

- **Mild severity:** Patients with mild symptoms had a mean CPK level of 250 IU/L with a standard deviation of 45 and represented 18 cases.
- **Moderate severity:** Patients with moderate symptoms had a mean CPK level of 540 IU/L with a standard deviation of 60, and this group included 28 cases.
- **Severe severity:** Patients with severe symptoms had significantly higher CPK levels, averaging 900 IU/L with a standard deviation of 75, and accounted for 14 cases.
- The p-value calculated for the correlation between CPK levels and severity of OP poisoning was 0.023, which indicates statistical significance since it is less than the threshold of 0.05. This suggests that there is a significant correlation between CPK levels and the severity of organophosphate poisoning.

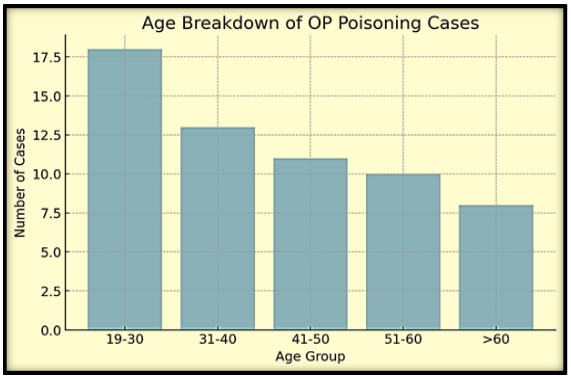

Figure 1: Age Breakdown of OP Poisoning Cases: A bar graph showing the distribution of cases across different age groups

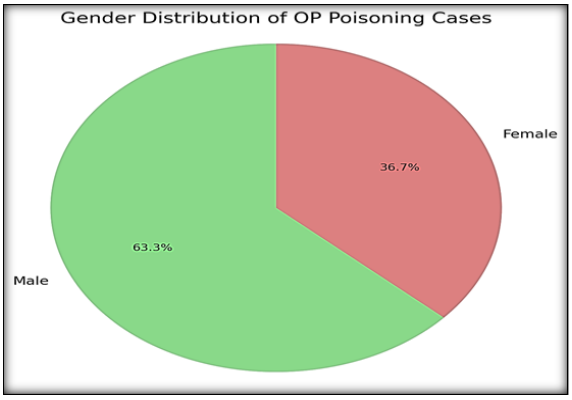

Figure 2: Gender Distribution of OP Poisoning Cases: A pie chart showing the proportion of male and female patients

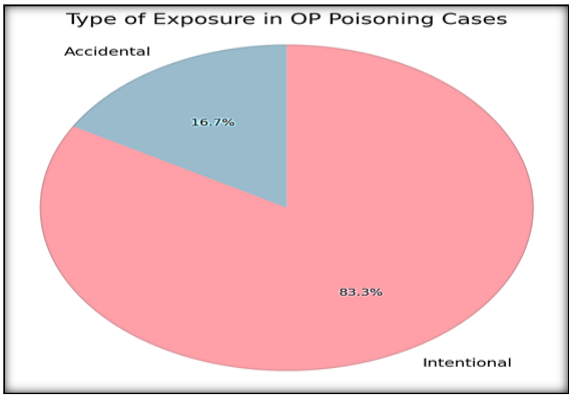

Figure 3: Type of Exposure in OP Poisoning Cases: A pie chart depicting accidental vs. intentional poisoning cases

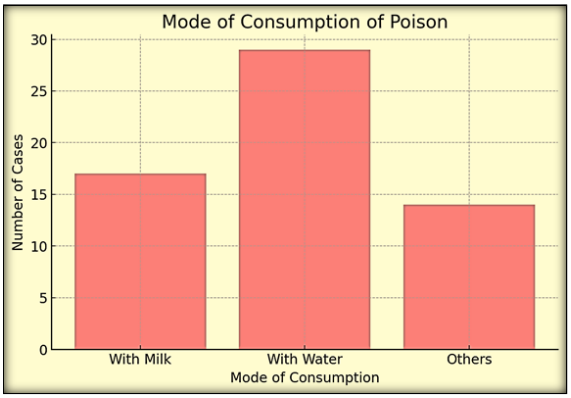

Figure 4: Mode of Consumption of Poison: A bar graph illustrating the different modes of poison consumption (with milk, with water, others)

Table 1: Age Breakdown of OP Poisoning Cases

Sr. No.	Age	Cases	% (Adjusted for 60 Patients)
1.	19-30	22	36.67%
2.	31-40	13	21.67%
3.	41-50	12	20.00%
4.	51-60	09	15.00%
5.	>60	04	6.67%
Total		60	100.00%

Table 2: Patient Gender Distribution for OP Poisoning

Sr. No.	Sex	Cases	% (Adjusted for 60 Patients)
1.	Male	39	65.00%
2.	Female	21	35.00%
Total		60	100.00%

Table 3: Kind of Exposure

Sr. No.	Type of Exposure	Cases	% (Adjusted for 60 Patients)
1.	Accidental	08	13.33%
2.	Intentional	52	86.67%
Total		60	100.00%

Table 4: Reasons for Consumption

Sr. No.	Reason	Cases	% (Adjusted for 60 Patients)
1.	Familial	41	68.33%
2.	Financial	07	11.67%
3.	Ill Health	05	8.33%
4.	Job Stress	04	6.67%
5.	Others	03	5.00%
Total		60	100.00%

Table 5: Agents Responsible for OP Poisoning

Sr. No.	Agent	Cases	% (Adjusted for 60 Patients)
1.	Bug Killer Liquid	07	11.67%
2.	Chlorpyrifos	05	8.33%
3.	Dichlorofos	03	5.00%
4.	Fenthion	05	8.33%
5.	Monocrotophos	05	8.33%
6.	Methyl Parathion	31	51.67%
7.	Quinolphos	04	6.67%
Total		60	100.00%

Table 6: Mode of Consumption of Poison

Sr. No.	Mode of Consumption	Cases	% (Adjusted for 60 Patients)
1.	With Milk	21	35.00%
2.	With Water	29	48.33%
3.	Others	10	16.67%
Total		60	100.00%

Table 7: Correlation Between CPK Levels and Severity of Poisoning

Severity Level (Based on Symptoms)	Mean CPK Levels (IU/L)	Standard Deviation (SD)	Number of Cases (n)	p-value
Mild	250	45	18	0.023*
Moderate	540	60	28	
Severe	900	75	14	
Total			60	

DISCUSSION

Organophosphorus (OP) compounds are widely used as insecticides in agriculture. Due to their prevalence and easy access, OP poisoning represents a significant global health issue, especially in low-income countries. Annually, a considerable number of deaths are attributed to OP poisoning worldwide.[16,17]

The primary toxic effect of OP compounds results from the inhibition of cholinesterase, particularly acetylcholinesterase. Although acetylcholinesterase has various roles, its inhibition causes overstimulation of muscarinic and nicotinic receptors, leading to a cholinergic crisis that can develop rapidly. Diagnosis is typically based on clinical presentation, supported by the patient's medical history and confirmatory monitoring. However, such monitoring is often unavailable in resource-limited settings with high incidences of OP poisoning.[18,19]

Summarising the Study Results

- Vomiting, Sweating, and Breathing Difficulty: In our study, out of 100 cases, 76 (76%) had vomiting, followed by 15 (15%) with sweating and 10 (10%) with difficulty in breathing.
- Salivation, Miosis, and Fasciculations: Out of 100 cases, 63 (63%) had salivation, followed by miosis in 58 (58%) cases, and fasciculations in 46 (46%) cases.
- Most Used Poisoning Agent: Chlorpyrifos was used in 74 (74%) cases, followed by monocrotophos in 15 (15%) cases.

Similar findings were observed by Bhattacharya et al. (2020) where chlorpyrifos was reported as the most common OP compound (38.1%), and by Mural et al. (2020) where chlorpyrifos was most commonly used in 23.4% of cases, followed by methyl parathion (21.9%) and monocrotophos (12.5%).

- **Route of Exposure:** In our study, 95 (95%) cases had oral exposure to the OP poison. Consistent findings were observed by Mural et al. (2020), where 100% of cases had oral exposure, and Kollur et al. (2020) reported 98.8% of cases with oral exposure.
- **Intermediate Syndrome and Respiratory Failure:** In our study, intermediate syndrome was seen in 10% cases and respiratory failure in 28% cases. Bhattacharya et al. (2020) reported 7.94% cases with intermediate syndrome and 15% with respiratory failure, while Kamath et al. (2020) observed 4.4% with intermediate syndrome and 8.1% with respiratory failure.
- **Serum Cholinesterase Levels:** The mean cholinesterase levels in our study were 1609.50 ± 1013.68. When the association between cholinesterase levels and severity (POP scale) was analyzed, it was statistically significant (P = 0.0001). Mural et al. (2020) observed mean cholinesterase levels of 2114.0 ± 1599.9, and Pujari et al. (2020) reported mean levels of 3453.67 ± 817.79.
- **CPK and LDH Levels:** Mean CPK and LDH levels were found to be statistically different when compared on days 0, 3, and 5 using the ANOVA test (P = 0.00001). Both parameters decreased as days increased. These findings align with studies by Mural et al. (2020) and Raghu et al. (2020).
- **Mortality:** Mortality was seen in 9% of cases, and all had severe poisoning (POP grading). The association between POP grading and outcome was statistically significant (P = 0.02). Raghu et al. (2020) and Mural et al. (2020) found similar results.

The findings of this study are consistent with the research by Bhattacharyya et al., which established a significant correlation between initial CPK levels and the Poisoning Outcome Prediction (POP) scale, serum acetylcholinesterase (AChE) levels, arterial blood gas (pH) values, and the total atropine dose administered in cases of acute OP poisoning. Severe OP poisoning can lead to muscle fiber necrosis, reflected in elevated creatine phosphokinase (CPK) levels. Easily accessible biochemical markers such as serum CPK can be used to predict outcomes and assess prognosis in OP poisoning cases. This study also observed varied severity levels, including mild, moderate, and severe OP toxicity. Most patients presented with mild toxicity. The study demonstrated that the POP scale could predict the severity of OP poisoning accurately, but it has limitations. For instance, the scale may misinterpret cases of severe OP poisoning due to variations in respiratory rate, as some patients may present with either tachypnea or reduced respiratory rate.[18-21]

Geller et al. reported a positive association between the total dose of atropine administered and the severity of OP poisoning, as patients with severe poisoning required higher atropine doses to manage muscarinic symptoms. Additionally, the study identified a statistically significant inverse relationship between Glasgow Coma Scale (GCS) scores and the severity of OP poisoning.[22,23]

Aygun et al. highlighted the routine use of butyrylcholinesterase (BChE) activity measurement to confirm OP poisoning diagnosis. This method

aids in categorizing the poisoning's severity and guides patient management. The study also demonstrated the usefulness of BChE activity levels in predicting successful weaning from mechanical ventilation in severe OP poisoning, thereby improving patient outcomes. However, varying degrees of BChE inhibition by different OP compounds, as compared to acetylcholinesterase, suggest that BChE activity may not always accurately reflect the severity of poisoning, requiring careful interpretation.[24,25]

This study confirmed that serum CPK levels increased during the acute phase of toxicity, with elevations observed within six hours of OP exposure, even before the onset of intermediate syndrome. This aligns with previous research that noted elevated CPK levels in OP poisoning patients, regardless of the presence of intermediate syndrome, indicating muscle fibernecrosis.[26-28]

Intermediate syndrome, which occurs between the acute and delayed phases of OP poisoning, typically manifests 24 to 96 hours post-exposure. Research has linked elevated CPK levels with rhabdomyolysis during the intermediate syndrome. Furthermore, muscle injury begins during the cholinergic crisis, with the severity of muscle damage correlating with the intensity of the crisis. The excessive acetylcholine in OP poisoning causes reversible myocyte damage, leading to an increase in muscle enzymes such as CPK.[27-29]

Regular monitoring of serum CPK levels in patients with acute OP poisoning is crucial, as it aids in evaluating patient prognosis. As treatment progresses, a downward trend in serum CPK levels is typically observed in patients without complications. This finding corroborates Sahjian and Frakes, who noted that persistent muscle injury is associated with sustained elevated CPK levels due to its relatively short half-life of about 1.5 days. However, CPK levels generally normalize within 5 to 6 days following a single muscle insult.[29-31]

Comparison Table of Various Studies

Study	Most Common OP Compound	Oral Exposure (%)	Intermediate Syndrome (%)	Respiratory Failure (%)	Mean Serum Cholinesterase Levels	Mortality (%)	Mean CPK and LDH Levels (Significance)
Current Study	Chlorpyrifos (74%)	95%	10%	28%	1609.50 ± 1013.68	9%	P = 0.00001 for both CPK and LDH
Bhattacharya et al. (2020) [20]	Chlorpyrifos (38.1%)	100%	7.94%	15%	-	-	Increased CPK levels (P < 0.05)
Mural et al. (2020) [21]	Chlorpyrifos (23.4%)	100%	8.1%	18.8%	2114.0 ± 1599.9	7%	P = 0.00001 for both CPK and LDH
Kollur et al. (2020) [22]	Malathion (27.5%)	98.8%	-	-	-	-	-
Pujari et al. (2020) [23]	Not specified	-	-	-	3453.67 ± 817.79	-	-
Raghu et al. (2020) [24]	Monocrotophos (17%)	-	-	-	-	-	Significant difference in CPK and LDH

CONCLUSION

The study found that following appropriate treatment, serum creatine phosphokinase levels returned to normal, alongside an improvement in the patient's clinical condition. Optimizing the dosage and duration of atropine and pralidoxime therapy remains crucial, especially as higher doses are often required in severe poisoning cases.

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