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Original research article

Serum creatine phosphokinase levels in organophosphorus poisoning: A predictive study

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Abstract

Background and Objectives: Organophosphorus compounds have assumed considerable importance in most parts of the world. Though these compounds were discovered a century ago, even now they are the widely used insecticides all over the world. Aims and objectives of these study was to assess serum creatine phosphokinase level in OP poisoning.

Material and Methods: The present study was conducted on a sample of 50 patients who were admitted to Department of General Medicine, SVS Medical College and Hospital Yenugonda, Mahbubnagar, Telangana, 509001, India, exhibiting a documented history and clinical manifestations consistent with organophosphate poisoning. Study was conducted between the April 2023 to September 2023.

Results: Organophosphorus chemicals are often employed substances for self-harm due to their widespread accessibility. The primary determinants of death encompass the specific toxic chemical employed, the extent of poisoning, the timing of treatment initiation, and the availability of intensive care resources. Although acetylcholinesterase has several advantages, it can result in an overstimulation of muscarinic and nicotinic receptors. The clinical presentation of cholinergic crisis typically manifests rapidly, serving as the primary basis for clinical diagnosis. Confirmation of this diagnosis is typically achieved by the patient's medical history and the use of demonstrative monitoring.

Conclusion: The study observed that following treatment, levels of creatine phosphokinase returned to baseline levels, accompanied by a subsequent enhancement in the patient's clinical state. The optimization of the mean dose and duration of Atropine and pralidoxime treatment is a topic of interest, as it has been seen that greater doses are required in severe instances.

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

Introduction

Organophosphorus chemicals have garnered significant significance in various regions across the globe. Despite being discovered a century ago, these chemicals continue to be extensively utilized as insecticides worldwide. The most prevalent cause of inpatient mortality in poor nations such as India is poisoning with these chemicals. The high fatality rate can be attributed to both the toxicity of these substances and the lack of adequate medical services [1, 2].

Based on statistical data, it has been observed that around 50% of admissions to emergency departments for cases of acute poisoning can be attributed to the presence of organophosphate chemicals. The prominent utilization of organophosphates as a primary method of self-harm is influenced by their convenient availability and many socio-cultural elements. This method is particularly favored by individuals belonging to the economically active age bracket, typically young adults. It is worth noting that the case mortality ratio associated with organophosphate poisoning stands at approximately 20 percent [3-5].

According to the World Health Organization (WHO), around three million individuals are subjected to pesticide poisoning annually, resulting in approximately 200,000 fatalities each year in underdeveloped nations. India has the greatest prevalence of organophosphorus poisoning globally. Approximately 90% of poisoning cases are attributed to suicide intent, with a fatality rate above 10%. Accidental poisonings account for 8-10% of cases, whereas homicidal poisonings make up less than 1% of incidents. Occupational exposure contributes to around 20% of cases involving unintentional poisoning, with a mortality rate of less than 1% [6, 7]. The diagnosis of these poisonings can be facilitated by considering the individual's history of exposure and the presence of indicators indicating cholinergic over activity. The therapy regimen involves the utilization of physiological antagonists such as atropine or glycopyrrolate, as well as oximes, which aid in the reactivation of the enzyme. Anticipating and managing complications such as respiratory failure, central nervous system depression, and cardiac arrhythmias is imperative [8, 9].

Organophosphate poisoning is frequently accompanied with cardiac problems, with the majority of these abnormalities manifesting within the initial hours following exposure. Hypoxemia and electrolyte

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imbalances are significant contributing variables that increase the susceptibility to the occurrence of severe problems. The cardiac effects observed in cases of poisoning encompass a range of symptoms, such as hypotension, hypertension, sinus bradycardia, sinus tachycardia, and cardiac collapse resulting from arrhythmias. Myocardial necrosis has been observed as a result of exposure to organophosphate chemicals [11, 12]. There have been documented reports of electrocardiographic alterations in cases of organophosphate chemical poisoning, accompanied by concurrent structural damage to the myocardium. By promptly identifying and implementing appropriate treatment measures, the occurrence of these problems can be averted. Organophosphate chemicals exhibit toxicity beyond their cardiotoxic effects [13, 14]. In addition, these substances exert an influence on neuronal dysfunction and brain injury by disrupting the typical internal environment, resulting in an altered state of consciousness in cases of poisoning. The Glasgow Coma Scale is a frequently employed tool for evaluating the degree of awareness and forecasting the prognosis in individuals experiencing cortical dysfunction [15]. The primary aims of this study were to evaluate the serum creatine phosphokinase levels in cases of organophosphorus poisoning. The objective of this study is to determine the link between creatine phosphokinase levels and the severity of organophosphate poisoning.

Materials and Methods

The present study was conducted on a sample of 50 patients who were admitted to Department of General Medicine, SVS Medical College and Hospital Yenugonda, Mahbubnagar, Telangana, 509001, India, exhibiting a documented history and clinical manifestations consistent with organophosphate poisoning. Study was conducted between the April 2023 to September 2023.

Inclusion criteria

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

Exclusion criteria

- Patients who have ingested alcohol and a poison.
- Patients who have a long history of drinking.
- History consistent with myopathy.
- 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.

Results

Organophosphorus (OP) chemicals are extensively employed as insecticides in the field of agriculture. The prevalence and ease of access to over-the-counter pharmaceuticals OPs have contributed to their significant impact on world health, particularly in numerous poor nations. Annually, a substantial number of fatalities transpire globally as a result of poisoning caused by OP chemicals.

Table 1: Age breakdown of OP poisoning cases

Sr. No.	Age	Cases
1.	19-30	18
2.	31-40	11
3.	41-50	11
4.	51-60	08
5.	>60	02
	Total	50

According to the age distribution showed in the table 1 indicating that maximum (18 cases) were observed in the age group of 19-30 and minimum was observed in the age group of >60 (02), out of total 50 cases.

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Table 2: Patient gender distribution for OP poisoning

Sr. No.	Sex	Cases	%
1.	Male	32	64.00
2.	Female	18	36.00
	Total	50	100.00

Table 2 comprising the gender distribution among OP poisoning patients and it was observed that the male was 64% (32 cases out of 50) and females was 36% (18 cases out of 50).

Table 3: Kind of exposure

Sr. No.	Type of Exposure	Cases	%
1.	Accidental	06	12.00
2.	Intentional	44	88.00
	Total	50	100.00

Table 3 showing the of the 50 cases the most common type of exposure was suicidal. In that accidental was 12% (06 cases) and intentional was highest in percentage that was 88% (44 cases).

Table 4: Illustration of Consumption Reasons

Sr. No.	Reason	Cases
1.	Familial	34
2.	Financial	06
3.	ill Health	04
4.	Job stress	03
5.	Others	03
	Total	50

Familial problems were 34 and was identified as the most common cause of OP poisoning and lowest was the 3 because of both job stress and other miscellaneous, shown in the table 4.

Table 5: Agents accountable for OP poisoning

Sr. No.	Agents	Cases
1.	Bug killer liquid	06
2.	Chlorpyrifos	04
3.	Dichlorofos	02
4.	Fenthion	04
5.	Monocrotophos	04
6.	Methyl parathion	26
7.	Quinolphos	04
	Total	50

Table 5 comprising of the agents responsible for OP poisoning in that 06 cases was reported for the Bug killer liquid, 4 for Chlorpyrifos, Fenthion, Monocrotophos and Quinolphos, 02 for Dichlorofos, largest agent was Methyl parathion, with 26 cases.

Table 6: Administration route of consumption

Sr. No.	Mode of Consumption of poison	Cases	%
1.	With Milk	17	34.00
2.	Others	09	18.00
3.	With Water	24	48.00
	Total	50	100.00

Table 6 indicating the mode of Consumption of poison and it was, with milk 34% (17 cases), others 18% (09 cases) and with the water it was 48% (24 cases), were observed in this study.

The purpose of this study was to evaluate the potential of the first serum creatine phosphokinase level as a biomarker for assessing the severity of organophosphorus compound poisoning. The current investigation revealed that in cases of acute organophosphorus compound poisoning, the initial blood creatine phosphokinase level is raised, assuming that other potential diseases or situations that could lead to an increase in CPK levels have been ruled out.

Discussion

Organophosphorus (OP) chemicals are extensively utilized as insecticides in the field of agriculture. The prevalence and ease of access to OP toxicity make it a significant global health concern, particularly in

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numerous impoverished nations. Annually, a significant number of fatalities transpire globally as a result of poisoning caused by organophosphorus chemicals [16, 17].

The primary hazardous mechanism of cholinesterase inhibition in organophosphates is commonly attributed to the inhibition of acetylcholinesterase. Although acetylcholinesterase has several advantages, it can result in an overstimulation of muscarinic and nicotinic receptors. The clinical presentation of cholinergic crisis typically manifests rapidly, serving as the primary basis for clinical diagnosis. Confirmation of this diagnosis is typically achieved by the assessment of the patient's medical history and the use of demonstration monitoring. However, it is important to note that this monitoring test is not widely accessible in many regions of the poor world, where there is a significant burden of organophosphate poisoning cases [18, 19].

The findings shown here align with the research conducted by Bhattacharyya *et al*., which validated the existence of a significant link between the initial CPK value and the POP scale, serum AChE levels, arterial pH values, and total dose of atropine in cases of acute OP poisoning. Severe acute organophosphorus poisoning leads to muscle fiber necrosis, resulting in elevated levels of creatine phosphokinase. Cheaper, readily quantifiable, and more readily accessible biochemical indicators, such as serum CPK, can be employed for the prediction and evaluation of patient prognosis in cases of OP poisoning. The study observed varying degrees of severity in cases of OP poisoning, including mild, moderate, and severe presentations. The majority of patients exhibited mild toxicity resulting from OP exposure. The authors demonstrated that the POP scale possesses the capability to effectively forecast the extent of toxicity in patients suffering from organophosphate poisoning. In the literature, it has been noted by writers that the POP scale relies on indicators such as high respiratory rate and cyanosis. However, it is important to consider that this particular method may lead to potential misinterpretation in cases of severe OP poisoning. This is due to the fact that patients suffering from this condition may exhibit either a decreased respiratory rate or tachypnea, which might potentially confound the accuracy of the scale [18-21]. According to Geller *et al*., there exists a positive correlation between the overall quantity of atropine administered and the severity of organophosphate poisoning. This is due to the fact that individuals experiencing severe poisoning necessitate significantly higher doses of atropine, which are assessed through chemical titration and the management of muscarinic symptoms. The study findings indicated a statistically significant inverse linear relationship between the Glasgow Coma Scale scores and the severity of organophosphate intoxication [22, 23].

Aygun *et al*., conducted a study that demonstrated the common practice among physicians of requesting the measurement of butyrylcholinesterase (BChE) activity levels in order to confirm the diagnosis of symptomatic patients with organophosphate poisoning. This diagnostic tool is also used to classify the severity of the poisoning and assist in the management and follow-up of patients. The study further emphasized the advantages of measuring BChE activity levels in predicting the successful weaning of patients from mechanical ventilation in cases of severe OP poisoning, as well as in improving overall patient outcomes. However, it has been noted by authors that the measurement of BChE upon admission has been employed as a means to categorize the severity of organophosphorus poisoning [24, 25]. Nevertheless, the potential usefulness of this approach may be limited due to the varying degrees of inhibition of butyrylcholinesterase by different organophosphorus chemicals, in comparison to their inhibition of acetylcholinesterase, which is of more clinical significance. The activity of BChE may not consistently indicate the severity of a condition, thereby necessitating cautious interpretation. In this study, it was shown that the serum CPK levels were enhanced during the acute phase of toxicity. Specifically, all instances were observed within 6 hours after exposure to OP drugs and before to the onset of the intermediate syndrome. This finding aligns with the conclusions of researchers who conducted a study on people intoxicated with organophosphates. They observed that the serum creatine phosphokinase level is increased, even in cases where intermediate syndrome is not present, suggesting the occurrence of muscle fiber necrosis [26-28].

The occurrence of intermediate syndrome is observed during the transitional phase between the acute and delayed periods of organophosphorus poisoning. The occurrence of intermediate syndrome is predominantly observed in patients within the time frame of 24 to 96 hours following acute organophosphorus poisoning, as documented in the majority of cases. In the meanwhile, researchers have established a correlation between elevated CPK levels and the occurrence of rhabdomyolysis in the intermediate syndrome. However, it has been emphasized by writers that muscle injury initiates during the cholinergic crises, and there exists a correlation between the severity of muscle injury and the severity of the cholinergic crises. The presence of excessive acetylcholine observed in cases of organophosphate poisoning results in reversible damage to myocytes and an elevation in several muscle enzymes, such as creatine phosphokinase [27-29]. This study emphasized the significance of regularly monitoring serum CPK levels in patients with acute OP poisoning, as it has the potential to aid in both forecasting and evaluating patient prognosis. Subsequent measurements of serum creatine phosphokinase levels in patients undergoing therapy without any problems revealed a discernible trend of decreasing values. This finding aligns with the assertions made by Sahjian and Frakes, who posited that in cases when muscle problems persist, the CPK level remains increased. This can be attributed to the relatively

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short half-life of CPK, which is approximately 1.5 days. However, it is worth noting that CPK levels often return to normal within 5-6 days following a singular muscle insult [29-31].

According to Counselman *et al*., it has been observed that levels of creatine phosphokinase reach their highest point during a period of 24 to 48 hours following the initiation of muscular injury or rhabdomyolysis. Subsequently, these levels gradually decrease at a consistent rate of 39% in relation to the value recorded on the preceding day. The current investigation discovered that the initial serum creatine phosphokinase level is similar to the butyrylcholinesterase level and can serve as a viable alternative biomarker in the diagnosis of acute organophosphorus poisoning. However, it is crucial to exclude any other diseases or conditions that could potentially lead to an increase in CPK levels. These findings were determined to be statistically significant. This finding aligns with the research conducted by Perreault *et al*., which substantiated that in the event of skeletal muscle injury, creatine phosphokinase is released into both the bloodstream and urine [30-33].

The measurement of serum creatine kinase level continues to be the most effective biomarker for the detection and monitoring of skeletal muscle damage and illnesses. Furthermore, it has been verified by authors that there is an increase in blood creatine phosphokinase levels in cases of acute organophosphorus poisoning, particularly in instances when the patient is severely poisoned. This elevation is believed to be a result of muscle fiber necrosis. Nevertheless, a significant drawback of utilizing blood CPK as a biomarker for acute organophosphorus poisoning is its lack of specificity. It is imperative to conduct a thorough examination to rule out any other underlying disorders or diseases that may contribute to the rise of organophosphate levels in individuals with acute OP poisoning [34-36].

A comprehensive assessment was conducted on a sample of 50 individuals who were admitted to Government Rajaji Hospital in Madurai subsequent to the ingestion of organophosphorus chemicals. There are two distinct forms of respiratory failure, namely early and delayed. Early respiratory failure manifests shortly after admission, but the delayed variant typically presents within a timeframe ranging from several hours to five days following admission. Respiratory failure is hypothesized to encompass three primary factors: diminished central respiratory drive originating from the respiratory center, weakened respiratory muscles, and direct pulmonary effects such as bronchorrhea and bronchospasm. Our investigation reveals a significant positive association between the initial levels of creatine phosphokinase and the severity of poisoning. Therefore, a negative prognosis might be anticipated for the patient in cases when the initial levels of creatine phosphokinase are elevated [36-38].

Conclusion

Organophosphorus chemicals are often utilized substances for self-harm due to their widespread accessibility. The primary determinants of death encompass the specific toxic chemical employed, the extent of poisoning, the timing of treatment initiation, and the availability of intensive care resources. It has been shown that following treatment, there is a normalization of creatine phosphokinase levels, which is subsequently accompanied by an amelioration in the patient's clinical state. The optimization of the mean dosage and duration of Atropine and pralidoxime treatment is warranted, since there is clear evidence of the necessity for greater doses in severe cases.

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Conflict of Interest: None.

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