

A STUDY OF THE PROGNOSTIC SIGNIFICANCE OF SERUM CREATINE PHOSPHOKINASE LEVEL IN ORGANOPHOSPHORUS COMPOUND POISONING PATIENTS

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Received : 11/01/2023
Received in revised form : 10/02/2023
Accepted : 23/02/2023

Keywords:

Serum creatine phosphokinase;
Organophosphorus; Poisoning.

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DOI: 10.47009/jamp.2023.5.2.95

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (2); 453-457



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Abstract

Background: Organophosphorus compounds (OPC) are easily accessible pesticides, which cause high morbidity and mortality among humans who are exposed. Serum acetylcholinesterase level (AChE) is usually used for assessing the severity of poisoning. In this study, we determine the role of serum creatine phosphokinase (CPK) level as an alternative prognostic marker. **Materials and Methods:** This prospective study was conducted at Government Mohan Kumaramangalam Medical College Hospital for two years, from December 2016 to June 2018. One hundred patients fulfilling the inclusion criteria were selected for the study. A detailed history and complete physical examination were made. Serum CPK and serum acetylcholinesterase were collected at admission and during follow-up in all patients. All routine investigations, including complete blood count, blood glucose and renal function tests were also done. The outcome studied would be survival with or without ventilator assistance and death. **Result:** Out of 100 patients enrolled in the study, 69% were males, and 31% were females. The maximum number of patients was reported in the ages of 21 to 30 and 31 to 40 years, representing 24% of each group of the total patients studied. The majority of patients were married (77%), were from rural areas (45%), and were farmers (36%). On admission, the pulse rate varied between 81 to 100 per minute. The respiratory rate was 16 to 26 in majority of patients (78%). A CPK level of more than >1400 was observed, with the highest values noted in the patients requiring ventilatory support (28%) and those who expired (81%). The AchE level of 501 to 1000 was observed with the most patients who died. **Conclusion:** There was a highly significant correlation between initial serum CPK levels and the severity of acute OPC poisoning.

INTRODUCTION

Organophosphorus compound (OPC) pesticide poisoning is common in developing countries like India. It has been used as a pesticide for over 70 years in agriculture. OPCs were first synthesized during the Second World War by German scientist Schrader.^[1] Organophosphorus compounds (OPCs) were later used as potential chemical warfare agents in the form of nerve gases.^[2]

WHO has estimated approximately 3,000,000 pesticide poisoning occurring yearly, causing more than 2,000,000 deaths globally. India, having a large

population involved in agriculture, OPC pesticides remain the main agent for crop protection. Because of wide availability and easy accessibility, it has become an agent of choice for self-poisoning.^[3] OP insecticides are irreversible inhibitors of carboxylic ester hydrolases, including acetylcholinesterase (AChE), erythrocyte cholinesterase (EChE), plasma or butyrylcholinesterase (BChE) and other nonspecific proteases. The primary toxicity from these compounds is due to excessive stimulation of muscarinic and nicotinic cholinergic receptors by the accumulated acetylcholine in the central and

autonomic nervous systems as well as at skeletal neuromuscular junctions.^[4]

The patients have varied presentations like bradycardia, meiosis, vomiting, diarrhoea, lacrimation, fasciculation, and rarely seizures indicating acetylcholine overactivity. The most common complication of OPC poisoning is respiratory failure leading to death. Other complications are acidosis, acute renal failure, arrhythmia, aspiration and coma.^[5] Hence, early recognition and prompt ventilator support can reduce the death rate and improve the outcome of the patients.

The most important aspect in treating OPC poisoning is triaging patients based on severity. However, very few biochemical markers indicate the severity of OPC poisoning.^[6] Serum RBC cholinesterase and plasma cholinesterase levels are reduced with poisoning, but measuring their levels is quite costly and may not be widely available. Hence there is a dire need to find out a cheap serum marker that can be affordable for triaging and monitoring all patients.^[7]

There are many quantifiable serum markers under study. A few among them are creatine phosphokinase (CPK), serum immunoglobulin, lactate dehydrogenase (LDH) and complements. Some studies have already proposed that serum CPK levels are increased in severe OPC poisoning, and there is a correlation with the outcome.^[7,8]

This study was done to assess the prognostic significance of serum CPK levels in OPC poisoning and to correlate it with serum acetylcholinesterase levels.

MATERIALS AND METHODS

This prospective study was conducted at Government Mohan Kumaramangalam Medical College Hospital for two years, from December 2016 to June 2018. One hundred patients fulfilling the inclusion criteria were selected for the study. Institutional ethics committee approval was obtained and written consent were taken before the start of the study.

Inclusion Criteria

Patients older than 18 years with a history of exposure to OP compound poison within 6 hours were included.

Exclusion Criteria

Patients with chronic renal disease, myopathy, myocardial infarction, epilepsy and trauma. Patients are on drugs like fibrates, statins, anticoagulants, aspirin, and dexamethasone; patients with a history of intramuscular injections after poisoning were excluded

After receiving informed consent from the patients, detailed history and complete physical examination were made. Sample for serum CPK level and serum acetylcholinesterase were collected at admission and during follow-up in all patients. All routine investigations, like complete blood count, blood glucose and renal function tests, were also done. The outcome would be survival with or without ventilator assistance and death.

The collected data were analysed with IBM.SPSS statistics software 23.0 Version. To describe the data, descriptive statistics, frequency analysis, and percentage analysis was used for categorical variables, and the mean and standard deviation were used for continuous variables. To find the significance in categorical data Chi-Square test was used similarly. Fisher's Exact was used if the expected cell frequency was less than 5. The probability value 0.05 is considered as significant level in the above statistical tools.

RESULTS

Out of 100 patients enrolled in the study, 69% were males, and 31% were females. They were aged above 18 years, and the maximum number of patients was reported in the age group of 21 to 30 years and 31 to 40 years, each with 24% of patients. The majority of patients were married (77%), were from rural areas (45%), and were farmers (36%), The pulse rate range of 81 to 100 (27%) and respiratory rate of 16 to 26 (78%) was observed in them (Table 1).

Table 1: Demographic and other variables of patients

Particulars	Observations N (%)	
	Male	Female
Gender	69 (69%)	31 (31%)
Age Group (years)	Upto 20 yrs	8 (8%)
	21 - 30 yrs	24 (24%)
	31 - 40 yrs	24 (24%)
	41 - 50 yrs	21 (21%)
	51 - 60 yrs	15 (15%)
	Above 60 yrs	8 (8%)
Marital status	Married	77 (77%)
	Unmarried	23 (23%)
Occupation	Coolie	10 (10%)
	Farmer	36 (36%)
	Homemaker	20 (20%)
	Private	9 (9%)
	Student	16 (16%)

	Unemployed	9 (9%)
Composition of poison	Chlorpyrifos	30 (30%)
	Dimethoate	28 (28%)
	Endosulfan	11 (11%)
	Malathion	9 (9%)
	Monocrotophos	22 (22%)
Area	Rural	45 (45%)
	Semiurban	27 (27%)
	Urban	28 (28%)
Pulse rate	40 - 60	21 (21%)
	61 - 80	51 (51%)
	81 - 100	27 (27%)
	> 100	1 (1%)
Respiratory rate	16 - 26	78 (78%)
	27 - 32	9 (9%)
	> 32	13 (13%)
Ventilation support	No	54 (54%)
	Yes	46 (46%)
Outcome	Dead	21 (21%)
	Discharged	79 (79%)

Oxygen saturation >95 and CPK level <350 were observed, with a maximum of 61% and 46% of patients, respectively. The Acetylcholinesterase level of more than 2500 was observed in the majority of patients (51%). In the present study, 46% of patients required ventilator support, and 21% patient mortality. A CPK level of more than >1400 was observed, with the highest value in patients requiring ventilation support (28%) and among those who expired (81%). The AchE level of 501 to 1000 was observed with the most patients who expired [Table 2].

Table 2: Observation of different evaluation parameters of patients

Particulars		Observations N (%)	
Oxygen Saturation (SpO ₂)	< 85	5 (5%)	
	85 - 90	14 (14%)	
	91 - 95	20 (20%)	
	> 95	61 (61%)	
Serum creatine phosphokinase (CPK)	< 350	46 (46%)	
	350 - 700	6 (6%)	
	701 - 1050	12 (12%)	
	1051 - 1400	8 (8%)	
	> 1400	28 (28%)	
Plasma Acetylcholinesterase (AChE)	501 - 1000	12 (12%)	
	1001 - 1500	15 (15%)	
	1501 - 2000	15 (15%)	
	2001 - 2500	7 (7%)	
	> 2500	51 (%)	
		Ventilator support	
CPK	<350	Yes 1 (2.2%)	No 45 (83.3%)
	350 - 700	1 (2.2%)	5 (9.3%)
	701 - 1050	9 (19.6%)	3 (5.6%)
	1051 - 1400	8 (17.4%)	0 (0%)
	> 1400	27 (58.7%)	1 (1.9%)
Comparison of serum CPK with the outcome	< 350	Death 0 (0%)	Discharge 46 (58.2%)
	350 - 700	1 (4.8%)	5 (6.3%)
	701 - 1050	0 (0.0%)	12 (15.2%)
	1051 - 1400	3 (14.3%)	5 (6.3%)
	> 1400	17 (81.0%)	11 (13.9%)
AChE	501 - 1000	9 (42.9%)	3 (3.8%)
	1001 - 1500	6 (28.6%)	9 (11.4%)
	1501 - 2000	4 (19%)	11 (13.9%)
	2001 - 2500	1 (4.8%)	6 (7.6%)
	> 2500	1 (4.8%)	50 (63.3%)

DISCUSSION

OPC pesticide poisoning is a major health hazard in developing countries like India. The incidence of OPC poisoning is increasing as a result of easy accessibility. More suicidal OPC poisoning were reported in both urban and rural populations in

recent literature. The present study was conducted for two years, from December 2016 to June 2018, in Govt Mohan Kumaramangalam Medical College Hospital Salem. The study was done after getting written consent from the patient. The study's epidemiology, clinical profile and outcome were compared with various distinguished literature.

In our study, most patients were 21 – 40 years (48%). In our study, maximum cases of poisoning was among patients younger than 40 years, which was very well comparable to studies done by Hassan et al., who reported 28.3% of patients aged 21 to 30 years.^[9] In this study, the incidence was more common in females with M: F of 0.9:1. Rayannavar et al. in their study also reported 67% male patients, which is close to our study observations.^[10]

The majority of patients were married (77%), from rural areas (45%), and farmers (36%), with pulse rates of 81 to 100 (27%) and respiratory rates of 16 to 26 (78%). Weissmann-Brenner et al. also reported similar findings in their investigations.^[11]

Chlorpyrifos (30%) was the most common OPC consumed in this study. It didn't correlate with any other research. Common signs in our study were miosis and fasciculations, which is comparable to Rayannavar et al.^[11] The mortality in the present study was 21 %, which is similar to Yamashita et al., who reported 23.5 % mortality in their investigations.^[12]

An increase in serum CPK correlates well with the severity of poisoning. A CPK level of more than >1400 was observed, with the highest level in those requiring ventilatory support (28%) and those who expired (81%). The AchE level range of 501 to 1000 was observed with the most patients who died. These results agree with Bhattacharyya et al., who confirmed a high correlation between initial CPK value and Peradeniya organophosphorus poisoning (POP) scale, serum AchE levels, arterial pH values and total dose of atropine in acute OPC poisoning.^[8] Muscle fibre necrosis and raised CPK levels occur in severe, acute OPC poisoning cases. So, cheaper, easily quantifiable and widely available biochemical markers concerning OPC poisoning, like serum CPK, can be used in predicting and assessing the prognosis of patients with OPC poisoning. Senanayake et al., illustrated that the POP scale can efficiently predict the severity of OPC-poisoned patients.^[13] Meanwhile, Eddleston et al. stated that the POP scale uses a high respiratory rate and cyanosis, and this approach is likely to be misleading in severe OPC poisoning as patients may have either a reduced respiratory rate or tachypnea.^[14]

In the present work, the elevated serum CPK levels were confirmed during the acute toxicity stage, i.e. all cases presented within 6 hours of exposure to OP compounds and before the development of the intermediate syndrome. This was in agreement with Bhattacharyya et al., who confirmed in their study on OPC poisoning patients that serum CPK level is elevated even in the absence of intermediate syndrome, presumably due to muscle fibre necrosis.^[8] Intermediate syndrome occurs in between the periods of acute and delayed OPC toxicity. Most reported cases of intermediate syndrome occur in patients 24–96 hours after acute OPC poisoning.

Meanwhile, De Wilde et al. linked the raised CPK levels to rhabdomyolysis in intermediate syndrome.^[15] But John et al. highlighted that muscle injury begins during the cholinergic crises, and the severity of muscle injury is correlated to the severity of the cholinergic crises. The excess acetylcholine seen in OPC poisoning leads to reversible myocyte injury and the rise of different muscle enzymes, including CPK.^[16]

However, the main disadvantage of serum CPK as a biomarker for acute OPC poisoning is its non-specificity. So, excluding other conditions and diseases that may cause its elevation in patients with acute OPC poisoning is mandatory. Sniderman stated that numerous factors influence CPK activity, so the suitability of CPK as a biomarker for diagnosing muscle injury and disease should be viewed with caution.^[18] Also, researchers illustrated that there are multiple causes of elevated CPK, which may affect its reliability as a biomarker.^[11-18]

CONCLUSION

OPC poisoning is one of the most common modes of suicidal death in our country. In our study, OPC poisoning among age groups between 21 to 40 years are more common. There is male preponderance in our study. Most of the patients consumed poison with suicidal intentions. Married people had more incidence of poisoning, and chlorpyrifos is the most common pesticide used. There was a good correlation between the elevation of CPK and the need for ventilatory support. Serum CPK level of more than 700IU/L correlated with the need for ventilator support and mortality. In this study, requirement for ventilator support was seen in 45% of patients. Mortality in our study was 21%. We found a high degree of correlation between initial CPK and mortality. Hence Serum CPK level can be used as an alternative biomarker in diagnosis or stratifying severity of acute OPC poisoning, as it is a cheap and easily available investigation, especially in developing countries.

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