

Serum Creatine Phosphokinase as Predictor of Intermediate Syndrome in Organophosphorus Poisoning

Lokesh N K¹, Shivakumar K M², Anikethan G V³

ABSTRACT

Introduction: Organophosphate compounds are one of the most common cause of poisoning worldwide. There are emerging option for severity assessment of OP compound poisoning like creatine phosphokinase level. These are cheap and easily quantifiable bio marker. Study aimed to assess serum creatine phosphokinase (CPK) level in OP poisoning and to find out the correlation of serum creatine phosphokinase (CPK) level with the severity of OP poisoning

Material and methods: 55 patients of acute organophosphorus poisoning admitted to medical wards and Intensive Medical Care Unit (IMCU) at Mandya Institute of Medical Science (MIMS) hospital, Mandya, during the period of July-2017 to December- 2017 was taken up for study considering the inclusion and exclusion criteria's. The clinical severity was assessed and categorized according to Peradeniya Organophosphorus Poisoning scale. A brief history and detailed clinical examination was performed and patients were categorized on the basis of POP score. Level of serum cholinesterase and serum CPK were estimated at admission and CPK level was measured on day 3 and day 5. The outcome of these patients was evaluated.

Results: Out of 55 patients, 63.6% were males and 36.4% were females. Majority of patients were in the age group 21 – 30 years. Dichlorvos was the most common compound used followed by Chlorpyrifos. 67.3% had mild, 16.4% had moderate and 16.4 had severe poisoning. Serial measurements of serum CPK levels showed significant correlation with the severity of acute OP poisoning patients. The CPK levels showed a sensitivity of 70% and a specificity of 82% with a positive predictive value of 95%.

Conclusion: High serum CPK level was associated with increased risk for intermediate syndrome and increased mortality. It can be used for assessing the severity of poisoning and early intervention like putting on mechanical ventilation and preventing mortality.

Keywords: Creatine Phosphokinase (CPK), Organophosphorus (OP), Peradeniya Organophosphorus Poisoning (POP) Score, Pseudocholinesterase.

producing an array of symptoms principal site being the peripheral nervous system². After ingestion, symptoms usually appear within 30-90 minutes and a maximum of 24hrs in case of compounds which are highly lipophilic and which require metabolic bioactivation³

The acronym SLUDGE— salivation, lacrimation, urination, defecation, gastrointestinal distress, and emesis are often taught to associate OP poisoning. These symptoms do not usually prompt an emergency attendant to consider OP poisoning unless there is a definite history of OP exposure⁴. Most important complication of OP compounds was acute cholinergic crisis and intermediate syndrome. The pathophysiology of intermediate syndrome was unclear.

Patients with acute OP poisoning are usually monitored by using serum AchE level, but its not specific and may not indicate severity of OP poisoning. There are emerging options for new cheaper and easily quantifiable biochemical markers in relation to OP poisoning like Creatine phosphokinase (CPK), lactate dehydrogenase (LDH), amylase and lipase. Estimation of CPK is easy and levels are increased both in acute phase and in intermediate syndrome due to muscle fibre necrosis. It has been reported that high serum CPK levels reflect the magnitude of acute muscle necrosis and is the best and most sensitive indicator of muscle injury⁹. There are several systems of grading of severity in acute organophosphorus poisoning.

Senanayake N¹⁰ proposed Peradeniya Organophosphorus Poisoning (POP) scale for grading the severity, which is based on five cardinal manifestations of organophosphorus poisoning namely pupillary constriction, fasciculations, heart rate, respiratory rate and level of consciousness. Each sign is given a score according to the severity and all are added up to assess the severity on a 1 to 11 scale. A score of 0-3 is graded as mild, 4-7 is graded as moderate and 8-11 is graded as severe poisoning. In countries like India OP compounds were most commonly used for agricultural purpose and easily availability of these compounds causing

INTRODUCTION

Poisoning has been known to be one of the leading causes of morbidity and mortality in the countries like India, Bangladesh and other Asian countries¹. Organophosphorus (OP) compounds are most commonly used poison. They are used in agriculture to control pests, weeds, or plants diseases and also for suicidal purposes³. Mechanism of action of organophosphorus compounds by inhibiting the enzyme acetylcholinesterase (AChE) which result in accumulation of acetylcholine at muscarinic and nicotinic receptors,

¹Assistant Professor, ²Professor, ³Assistant Professor, Department of Medicine, Mandya Institute of Medical Sciences, Mandya, Karnataka, India

Corresponding author: Dr Lokesh N K. 401-A Doctors Quarters, MIMS Mandya, 571401, Karnataka, India

How to cite this article: Lokesh N K, Shivakumar K M, Anikethan G V. Serum creatine phosphokinase as predictor of intermediate syndrome in organophosphorus poisoning. International Journal of Contemporary Medical Research 2018;5(6):F1-F4.

DOI: <http://dx.doi.org/10.21276/ijcmr.2018.5.6.10>

more health hazard.

Study aimed to assess serum creatine phosphokinase (CPK) level in OP poisoning and to find out the correlation of serum creatine phosphokinase (CPK) level with the severity of OP poisoning

MATERIAL AND METHODS

A Prospective observational study was conducted on 55 patients of acute organophosphorous poisoning admitted to medical wards and Intensive Medical Care Unit (IMCU) at Mandya Institute of Medical Science (MIMS) hospital, Mandya. The study was conducted from the period between July 2017 and Decemver- 2017, after getting approval from the institutional ethical committee. The informed consent was obtained from the attender of the patient's. Patients who had consumed organophosphorous compounds and directly admitted to our hospital without any prior treatment were included. The OP compound poisoning was confirmed by history and identifying the container brought by the patient attenders. Patients with history of muscle disease like myopathy and kidney disease, seizure disorder, malignancies, autoimmune diseases and patients taking medications like statins, fibrates and dexamethasone were excluded from the study, considering the CPK levels might be elevated in those

Age group	Total no of patients
16-20	2(3.6%)
21-30	19(34.5%)
31-40	18(32.%)
41-50	12(21.8%)
51-60	4(7.3%)

Table-1: Age wise distribution of study patients

Type of poison	Number of patients
Dichlorvos	20(36.4%)
Chlorpyrifos	15(27.3%)
Phorate	9(16.4%)
Monochrotophos	5(9.1%)
Profenophos	3(5.4%)
Quinalphos	3(5.4%)

Table-2: Distribution of the patients based on the type of OP compound poison consumed

POP scale	Number of study patients
Mild	37(67.3%)
Moderete	9(16.4%)
Severe	9(16.4%)

Table-3: Distribution of patients based on the severity of OPC poisoning by using the POP scale

POP score	Ps CHE level				
	Number	Minimum	Maximum	Mean	SD
Mild	37	1650	7690	5046.6	1741.5
Moderete	9	450	6000	2795.2	1662.8
Severe	9	426	600	487.2	72.86

Test applied: Kruskal wallis; P<0.01; HS

Table-4: Comparison of pseudocholinesterase with POP score

patients. A total of 55 study subjects were included for the study based on the above mentioned inclusion criteria.

The clinical severity was assessed and categorized according to Peradeniya Organophosphorous Poisoning scale. The levels of serum CPK (estimated by modified IFCC method) and plasma cholinesterase (estimated by kinetic, butrylthiocholine method) were measured on admission. Once the patient resuscitated, Blood sample was collected for routine laboratory and specific investigation. Depending upon the symptoms and severity of poisoning patients were treated with Inj. Atropine and Inj. Pralidoxime chloride.

STATISTICAL ANALYSIS

All the Data were entered in latest version of SPSS software. The mean and SD was derived for all the parametric variables and the Kruskal Wallis test and Spearman rank correlation was used to analyse data. P value less than 0.05 is statistically significant.

RESULTS

Total 150 cases of poisoning was admitted of which 55 matched the inclusion and exclusion criteria and were studied. Regarding the age and gender distribution, our study showed that majority of the patients from 21-30 yrs age group (35.4%), followed by 31-40 years age group (32.7%) (Table 1). Male (63.6%) outnumbered the females (36.4%).

In our study, the most common compound was Dichlorvos (36.4%) followed by chlorpyrifos (27.3%), Phorate (16.4%), Monocrotophos (9.1%), Profenofos (5.4%) Quinalphos (5.4%), Malathion (3.6%) (Table 2).

In our study, 37 patients (67.3%) were in the mild Peradeniya OP Poisoning score and 9 patients (16.4%) were in moderate score and 9 patients (16.4%) were in the severe score. Out of 55 patients 13 were intubated (23.6%). out of 55 patients 10 were developed intermediate syndrome. All patients who developed IMS put on mechanical ventilation (Table 3).

The study showed that pseudocholinesterase levels decreases with increase in severity of OP poisoning. The mean pseudocholinesterase level in mild, moderate and severe poisoning were 5046.6, 2795 and 487.2 IU/L respectively. This was found to be statistically highly significant (P<0.01) (Table-4).

Majority of patients had full improvement without any complications in our study and these patients had lower levels of creatine kinase. Higher mortality was observed in patients with higher creatine kinase levels. It was found to be statistically highly significant (P<0.01).

In our study, we observed that there was high degree of correlation between initial serum creatine kinase level and

POP SCORE	CPK level Day 1				
	Number	Minimum	Maximum	Mean	SD
Mild	37	90	435	188.4	129.3
Moderate	9	97	1200	432.8	340.1
Severe	9	124	1566	1010	458.5
Test applied: Kruskal wallis; P<0.01; HS					
POP score	CPK level Day 3				
	Number	Minimum	Maximum	Mean	SD
Mild	37	98	2311	435.8	478.6
Moderate	9	112	1897	823.6	572.4
Severe	9	680	3456	2264.2	826
Test applied: Kruskal wallis; P<0.01; HS					
POP score	CPK level Day 5				
	Number	Minimum	Maximum	Mean	SD
Mild	37	112	2432	480.2	604
Moderate	9	99	3422	889.6	1124.5
Severe	9	567	3212	2140.4	857.7
Test applied: Kruskal wallis; P<0.01; HS					

Table-5: Comparison of mean cpk level in different grades

Clinical profile	Raghavendra Mural et al ³ (%)	Kinathankaraiyan Nagarajan et al ⁴ (%)	Bhattacharyya K et al ¹ (%)	Present study (%)
Male	67	66	66.6	63.6
Female	33	34	33.4	36.4
Age group	21-40	30-40	21-40	21-40
Most common poison	Chlorpyrifos	Chlorpyrifos	Methyl parathion	Dichlorvos

Table-6: Comparison of different clinical profile with other studies

severity of poisoning and those patients with high initial CPK levels had fatal outcome. Mean CPK levels were highest in the death group on all 3 days followed by those patients who survived with intubation. This was found to be statistically highly significant (P<0.01) (Table-5).

DISCUSSION

Organophosphorus (OP) compounds are among the most commonly used pesticides by the farmers in their agriculture lands. Because of their wide use and easy accessibility its toxicity had become an important global health problem especially in many of the developing countries like India.

In our study, 63.6% of the population were males and 36.4% were females. This is in consensus with a study by Bhattacharyya K et al¹ at Calcutta medical college in which 66.6% were males and 33.3% were females. In a study by Raghavendra Mural et al³ in karnataka, showed 67% were males and 33% were female and study done by Kinathankaraiyan Nagarajan et al⁴ showed 66% were male and 34% were females.

Majority of patients in our study were in the age group of 21 – 40 years (67.2%) followed by 41-60 years age group (29.1%). This is in consensus with Bhattacharyya's¹ study which showed most patients in the age group of 21 – 40 years. Study done by Raghavendra Mural et al³ and by Kinathankaraiyan Nagarajan et al⁴ showed similar results. Majority of the patients in our study were in the third decade who would contribute to the economic status of the family and the reasons identified for consuming the poison were

financial loss, family disputes.

Dichlorvos (36.4%) was the most commonly used compound followed by chlorpyrophos (27.3%) and phorate (10.4%). In study done by Raghavendra murali et al³ showed Chlorpyrifos (23.4%) was the most commonly used compound followed by Methyl parathion (21.9%) and Dichlorvos (18.8%) (Table 6).

It has been shown by Senanayeke et al¹⁰ that POP score can efficiently predict the severity, morbidity and mortality of OP poisoned patients. 37 out of 55 (67.3), 9 out of 55 (16.4%) and 9 out of 55 (16.4%) were considered as mild moderate and severe cases of poisoning in our study.

The mean pseudocholinesterase levels were 5046.6, 2795, 487.2 (IU/L) in mild, moderate and severe cases of poisoning in our study. In Study done by Raghavendra Mural et al³ mean pseudocholinesterase levels were 2389, 1104.4, 237.5 (IU/L) in mild, moderate and severe cases of poisoning respectively. The mean CPK levels on day 1 were 188.4, 432.8 (IU/L) in mild and moderate cases of poisoning in our study. These results are in consensus with study done by Bhattacharyya et al¹ and Raghavendra Mural et al³.

The present study showed that there was a high degree of correlation between the serum CPK levels (third day level) and the severity of OP poisoning as illustrated by the positive correlation of CPK with POP score. These correlations are found to be statistically significant (p<0.001). Bhattacharyya et al¹, and Raghavendra Mural et al³ reported that there is a high degree of correlation between CPK levels and the severity of poisoning.

In our study, we found that high initial CPK level is associated with need for endotracheal intubation and mechanical ventilation and more chances of mortality. we found that high initial serum CPK levels is associated with severe degree of poisoning and is associated with complications and mortality. We also found that CPK levels normalises by day 5 in uncomplicated cases but continues to be high in complicated cases. The results were statistically significant ($P<0.001$).

CONCLUSION

In conclusion, this study found that Serum CPK can be used as an alternative biomarker in diagnosis or stratifying severity of acute OP poisoning, as it is cheap and easily available, especially in developing countries. Serial measurements of serum CPK levels in acute OP poisoning can predict the prognosis. To substantiate our findings more number of multicentric studies with larger sample size has to be conducted.

REFERENCE

1. Bhattacharyya k, Phaujdar S, Sarkar et al. Serum creatine kinase: A probable marker of severity in organophosphorus poisoning. *Toxicology International*: 2011;18:117–123.
2. Nermeen A. M. Hassan, Abdelmonem G. Madboly et al. Correlation between Serum Creatine Phosphokinase and Severity of Acute Organophosphorus Poisoning. *IOSR Journal Of Environmental Science, Toxicology And Food Technology (IOSR-JESTFT)*: 2013; 4:18-29.
3. Raghavendra Mural, Gopal Bajaj, Denny Mammen. Study of Level of Total Serum Creatine Phosphokinase as Prognostic Indicator in Acute Organophosphorus Poisoning: A Prospective Study. *International journal of contemporary medical research* 2015;4:578-582.
4. Kinathankaraiyan Nagarajan, Natesan Sudhan, Shankar Radhakrishnan. Serum Creatine Phosphokinase as aMarker of Severity in Organophosphorus Compound Poisoning. *Indian Journal of Basic and Applied Medical Research*; 2016;5:160-168.
5. Indian Council of Medical Research. Pesticide pollution trends and perspectives. *Indian Council Medical Research. Bulletin*. 2001;31:367–371.
6. Vanneste Y, Lison D. Biochemical changes associated with muscle fibre necrosis after experimental organophosphate poisoning. *Human Experimental Toxicology*. 1993;12:365–370.
7. G. Chetan Kumar, K. Bhuvana, P. N. Venkatarathnamma, and N. Sarala. Serum creatine phosphokinase as predictor of intermediate syndrome in organophosphorus poisoning. *Indian J Crit Care Medicine*. 2015;19: 384–387.
8. Roberts DM, Karunarathna A, Buckley NA, Manuweera G, Sheriff MH, Eddleston M. Influence of pesticide regulation on acute poisoning deaths in Sri Lanka. *Bulletin of the World Health Organization*. 2003;81:789-798.
9. John M, Oommen A, Zachariah A. Muscle injury in organophosphorus poisoning and its role in the development of intermediate syndrome.

Neurotoxicology. 2003;24:43-53.

10. Senanayake N, De Silva HJ, Karallillede L. A scale to assess severity of organophosphorus intoxication: POP scale. *Human Experimental Toxicology*. 1993;12:297-299

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 20-05-2018; **Accepted:** 23-06-2018; **Published:** 04-07-2018