Original Research Article

Prognostic significance of creatine phospokinase (CPK) levels in assessing the severity of organophosphorus poisoning compound poisoning

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Abstract

Background: OP toxicity is important global health problem especially in many developing countries. Acute pesticides exposure can be accident or suicide, occupational, bystander exposure, or exposure because of consumption of food items containing pesticide residues. Estimation of CPK is economical and levels are increased both in acute as well as in intermediate syndrome and can be used as a low budget, easily available prognostic marker for acute organophosphorus poisoning. Present study was aimed to assess prognostic significance of creatine phospokinase (CPK) levels in assessing the severity of organophosphorus poisoning compound poisoning. **Material and Methods:** This hospital based prospective, observational study conducted in cases of acute organophosphorus poisoning admitted to our hospital within 12 hours of consumption of the poison, >12 years age. **Results:** The majority of cases 139 (65%) were between the age group 20 to 40 years. The incidence of organophosphorus poisoning was more in males (137 patients, 64%) when compared to females (77 patients, 36%). The severity of the OPC poisoning was assessed clinically by Peradeniya Organophosphorus Poisoning (POP) scale. In the present study the mild form (51%) of OP poisoning was most common followed by moderate (29%) and severe form (18%). The CPK levels were much lower in the patients who had completely recovered when compared to the patients who had died and the difference in the levels were found to be statistically significant (p<.001). The CPK levels can be considered as a prognostic indicator in the patients who had consumed OPC poison. We noted a very strong negative correlation between serum CPK and serum acetylcholinesterase. **Conclusion:** Serum phosphokinase level has proved its efficacy as a prognosis marker in OP poisoning cases. It is cheap, easily available, especially in developing countries where EChE and BChE levels are not widely available in most of the laboratories.

Key Words: organophosphorus poisoning, serum cholinesterase, serum Creatine phosphokinase, severity, correlation.

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INTRODUCTION

Organophosphorus (OP) compounds have been used as pesticides and developed as chemical warfare nerve agents. They can be efficiently absorbed by inhalation, ingestion and skin penetration[1]. Because of their wide use and easy accessibility, OP toxicity is important global health problem especially in many developing countries. Every year, hundreds of thousands of deaths occur worldwide due to poisoning with OP compounds. According to WHO estimates, more than 90% of fatal poisoning cases are seen in middle and low income countries i.e. the developing countries in general and agricultural countries in particular. The estimated mortality rates with OPP in India are around 7-12 %[2].

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Acute pesticides exposure can be accident or suicide, occupational, bystander exposure, or exposure because of consumption of food items containing pesticide residues. The major toxicity of organophosphorus compound poisoning is due to inhibition of acetylcholinesterase, which leads to stimulation of muscuranic and nicotinic receptors. The accumulation of acetylcholine in nerve terminals, results in continued stimulation with subsequent paralysis of receptors. This is responsible for the clinical signs of OP compound poisoning. Laboratory evidence of OP poisoning is usually confirmed by measuring the decreases in the erythrocyte cholinesterase (EChE) and butyrylcholinesterase (BChE) activities. However, because of wide inter-individual variability, significant depression of the enzyme cholinesterase activity may occur but still fall within the "normal" range[3]. Also, estimation of either serum EChE or BChE levels is costly and not regularly performed in most laboratories[4]. There are emerging options for cheaper and/or easily quantifiable biochemical markers in relation to OP poisoning like creatine phosphokinase (CPK), lactate dehydrogenase (LDH) and serum immunoglobulins (IgG, IgA). But immunoglobulin assays, apart from being costly and difficult to perform in most laboratories, are often unreliable[5]. Estimation of CPK is economical and levels are increased both in acute as well as in intermediate syndrome and can be used as a low budget, easily available prognostic marker for acute organophosphorus poisoning[6,7]. Present study was aimed to assess prognostic significance of creatine phospokinase (CPK) levels in assessing the severity of organophosphorus poisoning compound poisoning.

MATERIAL AND METHODS

This hospital based prospective, observational study was conducted in Department of Medicine, M. R. Medical College. Study duration was of 1 year. Institutional ethical committee approval was obtained to carry out the study in the hospital.

Inclusion criteria: All cases of acute organophosphorus poisoning admitted to our hospital within 12 hours of consumption of the poison, >12 years age.

Exclusion criteria: The cases with indication of exposure to an entirely different poison other than OP poison, patients with OP poisoning and mixed with any other poison, chronic alcoholics patients, patients who had history of chronic liver disease, myopathy, history of malignancy, renal disease and history of intake of drugs like – statins, Fibrates, Dexamethasone, Aspirin, anticoagulants, frusemide were excluded from study. Written informed consent was taken from relatives for participation in present study. After initial resuscitation and stabilization of patients, blood samples were collected for serum creatine phosphokinase and serum cholinesterase, aseptically by a single prick, from a peripheral vein without tying any tourniquet. After that patients were treated with 2–PAM (Pralidoxime) (adult dose 1 to 2gm Intravenously followed by 0.5gm/hour infusion.) and initial dose of atropine 2 mg followed by bolus every 5 to 10 min or as an infusion until the signs of "atropinization"- heart rate >80/min and dilatation of initially constricted pupil occurred. Apart from serum CPK other relevant and routine investigations were done as per need. Follow up was kept till discharge. The collected data were tabulated and analyzed using statistical software. Continuous variables were presented as Mean ±SD. Categorical variables were expressed in actual numbers and percentages. Continuous variables were compared between mortality and survival by performing independent t-test. Correlation coefficient (r) was used to assess the relationship between initial CPK level and POP scale, Serum cholinesterase. P-value of <0.05 was considered as statistical significance.

RESULTS

After applying inclusion and exclusion criteria, total 213 patients were included in present study. Being a tertiary care hospital serving large area such large number of patients were noted. The majority of cases 139 (65%) were between the age group 20 to 40 years. The incidence of organophosphorus poisoning was more in males (137 patients, 64%) when compared to females (77 patients, 36%).

Table 1: Age and gender Distribution of Cases

Age Group (in years)	No. of patients (%)		
	Male	Female	Total
13-20	17 (8%)	24 (11%)	41 (19%)
21-30	65 (31%)	27 (13%)	92 (43%)
31-40	31 (15%)	16 (8%)	47 (22%)
41-50	13 (6%)	6 (3%)	19 (9%)
>50	10 (5%)	4 (2%)	14 (7%)
TOTAL	**136 (64%)**	**77 (36%)**	**213**

We noted that majority of poison consumption was intentional (92%) and only 8 % had accidental exposure. Among the various poisons consumed by the study subjects chlorpyrifos (62 %) and Monochrotophos (24%) were the most common form of organophosphorus poison in present study.

Table 2: Distribution of various OP compounds in poisoning

Type of poison	No. of patients	%
Chlorpyrifos	132	62%
Monochrotophos	51	24%
2% methyl parathion	17	8%
Dimethoate	5	2%
Profenophos	3	1%
Quinolphos	3	1%
Triazophos	2	1%

The severity of the OPC poisoning was assessed clinically by Peradeniya Organophosphorus Poisoning (POP) scale. Parameters which were taken into consideration like pupil size, respiratory rate, heart rate, fasciculations, level of consciousness and seizures. In the present study the mild form (51%) of OP poisoning was most common followed by moderate (29%) and severe form (18%).

Table 3: Distribution according to Severity of OP Poisoning (POP scale)

Severity of OP Poisoning	No. of patients	Percentage
Mild (0-3)	109	51%
Moderate (4-7)	61	29%
Severe (8-11)	39	18%
Total	**209**	**100%**

In patients who had consumed OP poison we measured serum cholinesterase and CPK. We correlated POP scale and serum CPK values and noted strong positive correlation between CPK and severity of poisoning. The CPK levels can also be used in classifying the severity of OPC poisoning. In the study subjects the CPK levels were lower in milder form of poisoning when compared to the moderate and severe form where CPK levels are high and is found to be statistically significant.

Table 4: CPK levels in the various forms of severity of OPC poisoning

Severity of OPC poisoning	CPK			P value
	Mean	SD	95% CI	
Mild	142.64	68.17	123.55 –179.16	0034
Moderate	516.91	179.98	455.24 – 575.42	
Severe	1217.21	523.62	1097.48 –1563.23	

Outcome of the patients were classified as completely recovered, recovered from intermediate syndrome, died due to intermediate syndrome and early death. 154 (72%) patients completely recovered. 37 (18 %) developed the intermediate syndrome, out of them 21 (10 %) recovered and 16 (8 %) patients died. In the present study death was reported in 18 % of patients. The CPK levels were much lower in the patients who had completely recovered when compared to the patients who had died and the difference in the levels were found to be statistically significant (p<.001). The CPK levels can be considered as a prognostic indicator in the patients who had consumed OPC poison.

Table 5: CPK levels in the various outcome forms of the study subjects

Outcome of the patient	No. of patients	CPK levels			P value
		Mean	SD	95% CI	
Completely recovered	154 (72 %)	321.16	179.13	236.75 – 361.1	<.0001
recovered from intermediate syndrome	21 (10 %)	652.81	194.92	571.36 – 695.34	
Died due to Intermediate syndrome	16 (8 %)	1021.56	343.73	847.82 –1152.4	
Death	22 (10 %)	1312.1	411.53	1091.67 – 1604.91	
Total			**213**		

We noted a very strong negative correlation between serum CPK and serum acetylcholinesterase.

Table 6: Correlation of various enzymes measured among patients

Study parameters	Pearson correlation coefficient	P value	Comments
Serum CPK and Acetylcholinesterase	r=-0.7528	0.004	High degree of negative co-relation

Out of 213 patients 51 required ventilator support, out of them 37 were died. Other complications like deranged RFT's noted in 21 patients, 34 patients had hypotension. Major causes of death were aspiration pneumonitis (37%), cardiac arrest (29 %), respiratory failure (18 %) and ARDS (16%).

DISCUSSION

OP compounds are prevalent worldwide in the agriculture as well as in the household gardens. Their easy availability combined with their sale over the counter has resulted in a gradual increase in poisoning with these agents. OP poisoning leads to three main syndromes: Acute cholinergic syndrome, intermediate syndrome (IMS), and OP induced delayed neuropathy (OPIDN)[8]. Organophosphorus compounds primarily inhibit esterase enzymes, including acetylcholinesterases present in synapses, red blood cell membranes, and butyrylcholinesterases in plasma. This results in accumulation of acetylcholine at synapses of the autonomic, neuromuscular and central nervous systems, causing overstimulation of effectors organs. Oximes like pralidoxime (PAM) cause AChEs to reactivate by binding to OPCs that have been bound to acetylcholinesterases. Deaths occur due to respiratory failure occurring in one of two distinct clinical syndromes: acute cholinergic respiratory failure or the intermediate syndrome. Delayed failure appears to be due to respiratory muscle weakness, but its pathophysiology is unclear[9]. The intermediate syndrome (IMS) from OP poisoning is noted to occur following the initial successful treatment of acute cholinergic syndrome with atropine. IMS is typically a syndrome of muscular paralysis that occurs in conscious patients, without cholinergic signs and symptoms, generally between 24 to 96 hours post ingestion. The muscles affected are generally the proximal limb muscles, motor cranial nerves and muscles of respiration, progressing to respiratory failure in the worst case scenario. Inadequate treatment with oximes may play a role in the development of IMS but the evidence is still lacking. Respiratory paralysis in IMS if identified early can reduce the need for ventilator support and appropriate treatment can be initiated at the earliest. Hence, identifying the patients at high risk for IMS may lead to a decrease in morbidity and mortality[10].In present study, among 80 patients of acute organophosphorous poisoning 136 (64%) were males and 77 (36%) were females and as in most other studies, male dominated females (M:F ratio 2.5:1).[8,9,10] The majority of cases 139 (65%) were between the age group 20 to 40 years This indicates that there is an increase incidence of organophosphorous compounds poisoning among the young people. These findings are similar to other studies[11,12]. There are several systems of grading of severity in acute organophosphorus poisoning. Senanayake N[13] 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.

Table 7: The Peradeniya OPC Poisoning scale

Parameters	Criteria	Score
Pupil size	>2mm	0
	<2mm	1
	Pin point	2
Respiratory rate	<20/min	0
	>20/min	1
	>20/min with central cyanosis	2
Heart rate	>60/min	0
	41 – 60/min	1
	<40/min	2
Fasciculation	None	0
	Present, generalized / continuous	1
	Both generalized and continuous	2
Level of Consciousness	Conscious and rationale	0
	Impaired response to verbal commands	1
	No response to verbal commands	2
Seizures	Absent	0
	Present	1

Note: 0 – 3 Mild Poisoning; 4 – 7 moderate poisoning; 8 – 11 severe poisoning

We correlated POP scale and serum CPK values and noted strong positive correlation between CPK and severity of poisoning. The correlation between initial CPK levels and poison severity was reported by Bhattacharyya *et al*, Nermeen *et al* and Sen R *et al*[5,14,15]. Patients with acute Organophosphorus poisoning are usually monitored by using serum acetylcholinesterase level which are expected to fall. It is not specific and does not correlate with the severity of poisoning and cannot be used as a prognostic indicator[5]. Estimation of CPK is easy and levels are increased both in acute phase and in intermediate syndrome is probably due to the presence of muscle fiber 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 injury[16].The increased muscle injury warrants increased the need for early ventilator care. Thus, keeping the half life of CPK in view, a repeat measurement of CPK level after 48 hours will help in early identification of ongoing muscle injury, need for early ventilator care and improves the prognosis. The CPK levels were much lower in the patients who had completely recovered when compared to the patients who had died and the difference in the levels were found to be statistically significant. We noted a very strong negative correlation between serum CPK and serum acetylcholinesterase. Similar findings were noted in other study[17].The disadvantage of serum CPK as a biomarker for acute organophosphorus compound poisoning is its nonspecificity. Other conditions like liver cell failure, muscular dystrophies

should be excluded before concluding on severity. Sniderman *et al* stated that many factors have influence on CPK activity, so the suitability of CPK as a biomarker for diagnosis of muscle injury and disease should be viewed with caution[18] .

CONCLUSION

Early diagnosis and treatment of OP poisoning cases is of paramount importance in reducing mortality and morbidity. Serum phosphokinase level has proved its efficacy as a prognosis marker in OP poisoning cases. it is cheap, easily available, especially in developing countries where EChE and BChE levels are not widely available in most of the laboratories.

REFERENCES

1. Chen Y, Organophosphate-induced brain damage: Mechanisms, neuropsychiatric and neurological consequences, and potential therapeutic strategies. Neurotoxicol, 33: 391–400(2012).
2. Selvaraj T, Sudharson T. Demographic and Clinical Profile of Organophosphorus Poisoning cases in a Medical College Hospital, Tamil Nadu. Indian Journal of Forensic and Community Medicine, April-June 2016; 3(2): 124-127.
3. Tanen DA. Organophosphorus and Carbamate Insecticides. In: Olson, K.R. (ed.), Poisoning and Drug Overdose. Lange medical books/McGraw-Hill, 5th Edn, New York, Chicago, Toronto, section II, (2007) pp: 291-295.
4. Bazire A, Gillon E, Lockridge O *et al*. The kinetic study of the inhibition of human cholinesterases by demeton-S-methyl shows that cholinesterase-based titration methods are not suitable for this organophosphate. Toxicol. In Vitro 2011; 25:754-759.
5. Bhattacharyya K, Phaujdar S, Sarkar R *et al*. Serum creatine phosphokinase: a probable marker of severity in organophosphorus poisoning. Toxicol. Interna 2011; 18(2):117-123.
6. Agarwal SB, Bhatnagar VK, Agarwal A, *et al*. Impairment in clinical indices in acute organophosphate insecticide poisoning patients in India. The Internet J of Toxicology 2007;4(1):1-6.
7. Hassan NAM, Madboly AG. Correlation between serum creatine phosphokinase and severity of acute organophosphorus poisoning. IOSR Journal of Environmental Science, Toxicology and Food Technology (IOSR-JESTFT) 2013:4(5):18-29.
8. Kalyanam B, Narayana S, Kamarthy P. A rare neurological complication of acute organophosphorous poisoning. Toxicol Int 2013;20:189‑91.
9. Eddleston M, Mohamed F, Davies JO, Eyer P, Worek F, Sheriff MH, *et al*. Respiratory failure in acute organophosphorus pesticide self-poisoning. QJM. 2006;99:513–22.
10. Yang CC, Deng JF. Intermediate syndrome following organophosphate insecticide poisoning. J Chin Med Assoc 2007;70:467‑72.
11. Bharath Kumar Guntheti, Shaik Khaja, S.S. Panda. A Study of Serum Cholinesterase Levels in Organo phosphorous Poisoning Cases. Journal of the Indian academy of forensic medicine, 2010; 32(4): 332-335.
12. S Agarwal, V Bhatnagar, A Agarwal, U Agarwal, K Venkaiah, S Nigam, S Kashyap. Impairment in Clinical Indices in Acute Organophosphate Insecticide Poisoning Patients in India. The Internet Journal of Toxicology., 2006; 4: 1-7.
13. Senanayake N, De Silva HJ, Karalliledde L. A scale to assess severity of organophosphorus intoxication: POP scale. Hum Exp Toxicol. 1993;12:297-99.
14. Nermeen A. M. Hassan N, Madboly A. Correlation between Serum Creatine Phosphokinase and Severity of Acute Organophosphorus Poisoning: A Prospective Clinical Study (2012-2013). IOSR Journal Of Environmental Science, Toxicology And Food Technology. 2013 Jan 1;4:18–29.
15. Sen R, Nayak J, Khadanga S. Study of serum cholinesterase, CPK and LDH as prognostic biomarkers in organophosphorus poisoning. International Journal of Medical Research and Review [Internet]. 2014 Jun 30. Available from: http://medresearch.in/index.php/IJMRR/article/view/101
16. Aygun D, Erenler AK, Karatas AD, Baydin A. Intermediate syndrome following Acute Organophosphate poisoning: Correlation with initial Serum levels of Muscle Enzymes. Basic Clin Pharmacol Toxicol. 2007;100:201-4.
17. Rode Vikram, Jadhav Nitin, Study of serum creatine phosphokinase levels as a prognostic biomarker among cases of organophosphate poisoning in a tertiary health care center, World Journal Of Pharmaceutical And Medical Research 2018,4(6), 195-203
18. Sniderman AD. Is there value in liver function test and creatine phosphokinase monitoring with statin use. Am J Cardiol. 2004;94(9A):30F-4.

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