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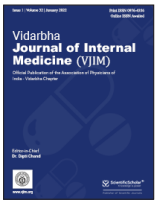

Original Article

Study of Levels of Creatine Phosphokinase and Lactate Dehydrogenase as Prognostic Markers in Acute Organophosphorus Poisoning

Tilottama Ramesh Parate[1], Shweta Vasant Madavi[1], Ramesh Parate[1]

[1]Department of General Medicine, Indira Gandhi Government Medical College, Nagpur, Maharashtra, India.

ABSTRACT

Objectives: Organophosphorus compound (OPC) poisoning is primarily a problem in developing countries. Its widespread use and easy availability have increased the likelihood of poisoning with these compounds. Serum cholinesterase levels are easier to estimate and usually depressed after organophosphorus (OP) poisoning. Peradeniya OP poisoning scale has not been studied much in the Indian scenario. It could be a simple and effective system to determine the need for ventilatory support early on in the course. Hence, this study was undertaken to assess the severity of OPC poisoning clinically using Peradeniya scoring and by estimating creatine phosphokinase (CPK) and lactate dehydrogenase (LDH) levels.

Material and Methods: A prospective observational study was performed among 100 cases of OP poisoning from January 2021 to October 2022. On patient's fulling, inclusion criteria were investigated with serum acetylcholinesterase at the time of admission, and periodic estimation of serum CPK and serum LDH was done on the day of admission and then on day three and day 5 of admission

Results: The CPK and LDH levels were significantly elevated in patients who developed respiratory failure and thus strongly correlated with clinical severity

Conclusion: Serum CPK and LDH show a strong degree of positive correlation with the severity of poisoning and can be used as a predictor of outcome in OP poisoning.

Keywords: Acetylcholinesterase, Creatine phosphokinase, Lactate dehydrogenase

INTRODUCTION

Organophosphorus compound (OPC) poisoning has assumed alarming proportions with an annual incidence of over 3 million patients in 1990. OPC poisoning is primarily a problem of the developing countries.[1] It is the most common medico toxic emergency in India, thus an important indication for emergrncy admission in most hospitals throughout the country. OPCs were first developed by Schrader shortly before and during the Second World War. They were first used as an agricultural insecticide and later as potential chemical warfare agents.[2]

OPCs are used as pesticides, herbicides and chemical warfare agents in the form of nerve gases.[2] Its widespread use and easy availability have increased the likelihood of poisoning with these compounds. Although poisoning can result from occupational exposure or accidental ingestion, in most cases, there is suicidal intent. Their common availability renders organophosphorus (OP) insecticide poisoning a worldwide health problem affecting millions of patients. India is a tropical country where agriculture forms the backbone of the nation. More than 60% of Indians are farmers. This being the fact, pesticides are the most frequent hazardous compounds that farmers are exposed to, OPC being most common in addition to the accidental intoxication from the use of these compounds as agricultural insecticides; these agents are employed frequently for suicidal and homicidal purposes largely due to their easy availability at the moment of frustration and low cost.[3]

The World Health Organization estimates that approximately 3 million pesticide poisonings occur annually worldwide and cause more than 220,000 deaths. Developing countries such as India and Sri Lanka report alarming rates of toxicity and death.[4]

OP poisoning causes what is known as the 'suicide impulse,' which leads to high levels of suicide in some sectors of the

***Corresponding author:** Shweta Vasant Madavi, Department of General Medicine, Indira Gandhi Government Medical College, Nagpur, Maharashtra, India. shwetavmadavi@gmail.com

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agricultural industry. These compounds act by inhibiting the enzyme acetylcholinesterase (AchE), which results in the accumulation of acetylcholine at muscarinic and nicotinic receptors, producing an array of symptoms principal site being the peripheral nervous system.[5]

Lactate dehydrogenase (LDH) is an enzyme that catalyses the interconversion of lactic acid and pyruvic acid. It is a hydrogen transfer enzyme that uses the coenzyme NAD+. LDH is widely distributed in the body.[6] Creatine kinase (CK), also known as creatine phosphokinase (CPK) or phosphocreatine kinase, is an enzyme expressed by various tissues and cell types. CK catalyses the interconversion of phosphocreatine (or creatine phosphate) to creatine.[7]

Patients with acute OP poisoning are usually monitored using serum AchE level, which is expected to fall. It is not specific, does not correlate with the severity of poisoning, and cannot be used as a prognostic indicator. There are emerging options for new, cheaper, and/or easily quantifiable biochemical markers in relation to OP poisoning, like CPK.[8,9]

Estimation of CPK is easy, and levels are increased both in the 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 are the best and most sensitive indicator of muscle injury.[10,11]

Most of the studies have shown that though serum cholinesterase can be used as a diagnostic marker, its role is minimal as a prognostic marker.[10,12] Hence, cheap and easily measurable biomarkers having prognostic value are the need of the hour.[13-15] It was proved beyond doubt that rhabdomyonecrosis occurs in animals after experimental poisoning by OP compounds.[16]

Mortality ranges from 4% to 30% in Indian studies. Respiratory failure is the most common complication of OP poisoning, leading to death. Early recognition and prompt ventilatory support may improve survival. Due to the limited availability of resources, all OP poisoning patients are not managed in intensive care units in the Indian setup. It is, therefore, important that clinical features and criteria to predict the need for ventilatory support be identified at the initial examination.[3]

Serum cholinesterase levels are easier to estimate and usually depressed after OP poisoning. Peradeniya OP poisoning scale has not been studied much in the Indian scenario. It could be a simple and effective system to determine the need for ventilatory support early on in the course. Hence, this study was undertaken to assess the severity of OPC poisoning clinically using Peradeniya scoring and by estimating CPK and LDH levels.

MATERIAL AND METHODS

A prospective observational study was performed among 100 cases of OP poisoning from January 2021 to October 2022 in MICU and general medicine wards in the Department of General Medicine, Indira Gandhi Government Medical College, Nagpur, who fulfilled the inclusion and exclusion criteria. The Institutional Ethical Committee clearance was obtained before the commencement of the study.

Inclusion criteria

OP poisoning suspected cases ≥12 years of age within six hours of consumption, history of ingestion or inhalation or contact with OPCs, and those who gave informed consent were included in the study.

Exclusion criteria

Patients with a history of consumption of OPC mixed with any other poison or alcohol, patients with a history of chronic alcoholism or with other coexisting illnesses (myopathy chronic renal disease, epilepsy, myocarditis, haemoglobinopathies, autoimmune diseases or malignancy or pregnancy), who had trauma or received intramuscular (I/M) injection and cardiopulmonary resuscitation recently and who are below 12 years of age were excluded from the study.

Methodology

The type of poisoning was ascertained by containers brought by relatives in the setting of clinical and biochemical features of OPC poisoning. The Peradeniya OP poisoning scale was calculated, and patients were classified. Serum cholinesterase was estimated on the day of admission; serum CPK and serum LDH will be done on the day of admission and then on day three and day 5 of admission. Along with the biochemical analysis, the patient was followed up for clinical outcomes such as complete recovery, respiratory failure, and death.

Statistical analysis

Data were coded and analysed in statistical software SPSS version 26.

Descriptive statistics were calculated to summarise quantitative variables by mean and standard deviation and qualitative variables by frequency and percentages.

Inferential statistics included confidence interval and test of significance (*P*-value), and appropriate tests were applied to analyse data.

RESULTS

In our study, the majority, 38 (38%) cases, were in the age group of 11–20 years, followed by 27 (27%) in 21–30 years,

followed by 17 (17%) cases in 31–40 years of age. The mean age was 27.61 ± 12.11 years, ranging from 12 to 60 years. About 82% of the patients were within 40 years of age. Maximum cases 56 (56%) were female. Male: female ratio was 1.27:1. The gender-wise incidence of poisoning in the present study did not show a significant difference.

The majority, 73 (73%) cases, were literate in our study, and the majority, 57 (57%) cases, lived in urban areas.

Out of 100 cases, 92 (92%) cases had suicidal exposure. As OPCs are generally available ready hand as pesticides, open access to these compounds at pesticide shops may be the reason for OPCs to be used as a common mode of suicidal attempt.

Out of 100 cases, a maximum of 74 (74%) cases used chlorpyrifos, followed by monocrotophos in 15 (15%) cases. Among the majority of cases, 95 (95%) had an oral route for OP poison.

On admission, a maximum cases 58 (58%) cases were in severe grade of poisoning, followed by moderate poisoning in 35 (35%) cases, according to the Peradeniya OP poisoning scale. The majority, 42 (42%), had serum cholinesterase levels ≤1000, followed by 29 (29%) cases with 1001–2000 levels.

The distribution of study subjects as per mean values of parameters measured is shown in Table 1. When mean CPK levels were compared on days 0, 3, and 5, they were found to be statistically different after applying the Analysis of Variance (ANOVA) test ($P = 0.00001$). Similarly, when mean LDH levels were compared on days 0, 3, and 5, they were found to be statistically different after applying the ANOVA test. ($P = 0.00001$). Values of both parameters decreased as the day increased.

A comparison of the mean values of CPK and Paradeniya organophosphorus poisoning grading of OP poisoning is shown in Table 2. There was a statistically significant difference in mean CPK values on days 0, 3, and 5 day in terms of POP grading severity in all three grades ($P = 0.00001$).

A comparison of the mean values of LDH and Peradeniya organophosphorus poisoning grading of OP poisoning is shown in Table 3.

Table 1: Distribution of study subjects as per mean values of parameters measured.

Parameters	Mean±SD	ANOVA test *P*-value
Cholinesterase levels	1609.50±1013.68	-
CPK levels day 0	249.10±78.05	0.00001*
CPK levels day 3	221.20±65.27	
CPK levels day 5	197.60±58.57	
LDH levels day 0	423.15±78.55	0.00001*
LDH levels day 3	398±71.17	
LDH levels day 5	375.20±65.39	

LDH: Lactate dehydrogenase, CPK: Creatine phosphokinase, SD: Standard deviation, ANOVA: Analysis of Variance. *: Significance

The intermediate syndrome was seen in 10 (10%) cases. When mean LDH and CPK levels were compared in cases with and without intermediate syndrome, we found higher levels in cases with intermediate syndrome. This finding was statistically significant ($P = 0.001$).

The distribution of study subjects as per POP grading and respiratory failure is shown in Table 4. When the Chi-square test was applied to see the association between POP grading and respiratory failure, it was found to be statistically significant ($P = 0.00001$).

DISCUSSION

OP poisoning is a major health problem worldwide and one of the most common causes of morbidity and mortality, particularly in developing countries. The prognosis depends on the time lag between exposure and the onset of management. With an increase in the use of this compound for industrial and agricultural purposes and due to easy accessibility and low cost, they are becoming a major source of health hazards. Early identification, diagnosis, and appropriate management are vital to reduce mortality.

In our study, out of 100 cases, 76 (76%) cases had vomiting, followed by 15 (15%) cases with sweating and 10 (10%) with difficulty in breathing.

In the present study, out of 100 cases, 6 (63%) cases had salivation, followed by miosis in 58 (58%) followed by fasciculations in 46 (46%) cases.

In our study, out of 100 cases, a maximum of 74 (74%) cases used chlorpyrifos, followed by monocrotophos in 15 (15%) cases.

Similar findings were seen in the study by Bhattacharya *et al.*[8] where the most common OP compound found to be abused was chlorpyrifos in 24 (38.1%) patients, which is an agricultural pesticide.

While Kollur *et al.*[17] observed malathion in 22 patients (27.5%) as the most consumed poison, followed by monocrotophos in 21 patients (26.25%), and 18 patients (22.5%) consumed dichlorvos. Another study by Mural *et al.*[18] found the most used compound as chlorpyrifos (23.4%), followed by methyl parathion (21.9%), dichlorvos (18.8%), and monocrotofos (12.5%) in their study which is similar to our study.

Raghu *et al.*[19] observed that the most common compound ingested was monochrotophos 17% followed by dichlorvos 13.8%, chlorpyrifos 12.8%, profenofos 8.5% and dimethoate 7.4%.

In our study, the maximum cases, 95 (95%), had an oral route for OP poison.

Table 2: Comparison of mean values of CPK and POP grading of OP poisoning.

Poisoning severity (POP scale)	CPK levels day 0	CPK levels day 3	CPK levels day 5	ANOVA test *P*-value
Mild				
Mean±SD	105±31.49	90.71±26.20	80±22.91	0.00001*
Moderate				
Mean±SD	198.43±29.97	187.43±28.73	175.29±27.83	0.00001*
Severe				
Mean±SD	297.07±58.93	257.33±52.11	225.26±51.56	0.00001*

CPK: Creatine phosphokinase, OP: Organophosphorus, ANOVA: Analysis of Variance, SD: Standard deviation, POP: Peradeniya organophosphorus poisoning, *: Significance

Table 3: Comparison of mean values of LDH and POP grading of OP poisoning.

Poisoning severity (POP scale)	LDH levels day 0	LDH levels day 3	LDH levels day 5	ANOVA test *P*-value
Mild				
Mean ± SD	292.14 ± 31.73	281.43 ± 24.95	277.86 ± 23.78	0.000*
Moderate				
Mean ± SD	369.57 ± 56.37	352.29 ± 52.20	335.57 ± 50.29	0.000*
Severe				
Mean ± SD	471.29 ± 49.87	439.66 ± 48.87	410.86 ± 49.37	0.000*

LDH: Lactate dehydrogenase, OP: Organophosphorus, ANOVA: Analysis of Variance, SD: Standard deviation, POP: Peradeniya organophosphorus poisoning, *: Significance

Table 4: Distribution of study subjects as per POP grading and respiratory failure.

Respiratory failure	Poisoning severity (POP scale)			Total	*P*-value
	Mild (%)	Moderate (%)	Severe (%)		
No	07 (100)	35 (100)	30 (51.7)	72 (72)	0.00001*
Yes	0 (0)	0 (0)	28 (48.30)	28 (28)	
Total	07 (100)	35 (100)	58 (100)	100	

POP: Peradeniya organophosphorus poisoning, *: Significance

Consistent findings were seen in the study by Mural *et al.*[18] where 100% of cases in our study were suicidal, and the route of exposure was oral and Kollur *et al.*[17] had 98.8% cases with oral exposure.

In our study, intermediate syndrome was seen in 10 (10%) cases. Respiratory failure was seen in 28 (28%) cases. When mean LDH and CPK levels were compared in cases with and without intermediate syndrome, we found higher levels in cases with intermediate syndrome. This finding was statistically significant (P = 0.001). Bhattacharya *et al.*[8] found 7.94% cases with intermediate syndrome and 15% cases with respiratory failure, which is higher than our study findings, while Kamath *et al.*[20] observed in 4.4% of cases with intermediate syndrome and respiratory failure in 8.1% of cases, which is lower than our study.

In our study, the majority, 42 (42%), had serum cholinesterase levels ≤1000, followed by 29 (29%) cases with 1001–2000 levels. The mean serum cholinesterase levels in our study were 1609.50 ± 1013.68. When the association between cholinesterase levels and severity based on the POP scale was seen using the Chi-square test, it was found to be statistically significant (P = 0.0001). Mural *et al.*[18] observed mean serum cholinesterase levels as 2114.0 ± 1599.9. Pujar*i et al.*[21] found mean serum cholinesterase levels as 3453.67 ± 817.79. The findings are higher than our study.

In our study, when mean CPK levels were compared on days 0, 3, and 5, they were found to be statistically different after applying the ANOVA test (P = 0.00001). Similarly, when mean LDH levels were compared on days 0, 3, and 5, they were found to be statistically different after applying the ANOVA test (P = 0.00001). Values of both parameters decreased as the day increased.

There was a statistically significant difference in mean CPK values on days 0, 3, and 5 day in terms of POP grading severity in all three grades (P = 0.00001). Furthermore, there was a statistically significant difference in mean LDH values on days 0, 3, and 5 day in terms of POP grading severity in all

three grades ($P = 0.00001$).

Studies by Mural *et al*.[18] and Raghu *et al*.[19] and Sangeetha *et al*.[22] observed similar results as our study, with significant differences in mean CPK levels and LDH levels according to the severity of the disease.

Bhattacharya *et al*.[8] observed reduction in CPK values with treatment in mild cases as significant, but the changes in the moderate ($P > 0.05$) and the severe ($P > 0.05$) groups were not so.

Other studies by Hariprasad *et al*.,[23] have found increased LDH activity in the serum of patients with OP poisoning. In Agarwal *et al*.[13] study, serum LDH activity was significantly elevated ($P \leq 0.01$) in poisoning cases, indicating muscular functional impairment due to OP toxicity. Sangeetha *et al*.[22] observed that serum LDH levels can be an efficient biomarker in case of acute OP poisoning. 19 In Rabha *et al*.[24] study, serum LDH levels, however, did not correlate in predicting mortality in poisoning cases.

In the present study, mortality was seen in 9% of cases. All of these cases had severe grades of poisoning, according to POP. There was a statistically significant association between POP grading and outcome, as all cases who died had severe POP grading ($P = 0.02$). Similar results were seen by Raghu *et al*.[19] and Mural *et al*.[18]

CONCLUSION

Maximum cases (58%) cases were in severe grade of poisoning, followed by moderate poisoning (35%) cases. In our study, mortality was only 9%. We found an association between the severity of OP poisoning according to POP grading and LDH CPK levels. Respiratory failure is the most common cause of death in OP poisoning. Although ventilators are a boon to patients with respiratory failure, early identification and intensive management are vital in reducing mortality. Cholinesterase levels may be considered a marker of OP poisoning since it enables the early recognition of severity and also helps to identify those at risk of developing the delayed complications of OP poisoning.

Ethical approval

The research/study complied with the Helsinki Declaration of 1964.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Mogda KM, Kashoury A, Rashed MA. Oxidative and Biochemical Alterations Induced by Profenofos Insecticide in Rats. Nat Sci 2009;7:1-15.
2. Bolognesi C. Genotoxicity of Pesticides: A Review of Human Biomonitoring Studies. Mut Res 2003;543:251-72.
3. Taylor P. Anticholinesterase Agents. In: Hardman JG, Limbird LE, Molinoff PB, Ruddon RW, editors. Goodman and Gilman's the Pharmacological Basis of Therapeutics. 9th ed. United States: McGraw Hill Medical; 1996. p. 161-76.
4. World Health Organization. World Health Report 2004. Geneva: WHO; 2004.
5. Sen R, Nayak J, Khadanga S. Study of Serum Cholinesterase, CPK and LDH as Prognostic Biomarkers in Organophosphorus Poisoning. Int J Med Res Rev 2014;2:185-9.
6. Krefetz RG, McMillin GA. Enzymes. In: Bishop ML, Fody EP, Schoeff L, editors. Clinical Chemistry. 5th ed. United States: Lippincott Williams and Wilkins; 2005. p. 236-61.
7. Satyanarayana U, Chakrapani U. Enzymes. In: Biochemistry. 3rd ed. Kolkata: Books and Allied Pvt Ltd.; 2009. p. 85-115.
8. Bhattacharya K, Phaujdar S, Sarkar R, Mullick OM. Serum Creatine Phosphokinase: A Probable Marker of Severity in Organophosphorus Poisoning. Toxicol Int 2011;18:117-23.
9. Hassan NA, Madboly AG. Correlation between Serum Creatine Phosphokinase and Severity of Acute Organophosphorus Poisoning: A Prospective Clinical Study (2012-2013). J Environ Sci Toxicol Food Technol 2013;4:18-29.
10. 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.
11. 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.
12. Aravanapavananthan TS. Serum Pseudocholinesterase Estimation in the Management of Organophosphate Poisoning Cases and the Effect of PAM on Regenerating It. Singapore Med J 1987;28:166-71.
13. Agarwal S, Bhatnagar V, Agarwal A, Agarwal U, Venkaiah K, Nigam S, *et al*. Impairment in Clinical Indices in Acute Organophosphate Insecticide Poisoning Patients in India. Internet J Toxicol 2006;4:6.
14. Lee WC, Yang CC, Deng JF, Wu ML, Ger J, Lin HC, *et al*. The Clinical Significance of Hyperamylasaemia

in Organophosphate Poisoning. J Toxicol Clin Toxicol 1998;36:673-81.
15. Sahin I, Onbasi K, Sahin H, Karakaya C, Ustun Y, Noyan T. The Prevalence of Pancreatitis in Organophosphate Poisonings. Hum Exp Toxicol 2000;21:175-7.
16. Vanneste Y, Lison D. Biochemical Changes Associated with Muscle Fibre Necrosis after Experimental Organophosphate Poisoning. Hum Exp Toxicol 1993;12:365-70.
17. Kollur BS, Mulimani MS. Study of Levels of Serum Creatine Phosphokinase and Liver Enzymes as a Prognostic Indicators in Acute Organophosphorus Poisoning. Int J Clin Biomed Res 2018;4:57-61.
18. Mural R, Bajaj G, Mammen D. Study of Level of Total Serum Creatine Phosphokinase as Prognostic Indicator in Acute Organophosphorus Poisoning: A Prospective Study. Int J Contemp Med Res 2017;4:578-82.
19. Raghu G, Gangannavar AA, Kumar BK, Rajoor U. Study of Serum Creatinine Phosphokinase and Serum Lactate Dehydrgenase as Prognostic Markers in Organophosphorus Poisoning. Int J Adv Med 2020;7:1125-30.
20. Kamath SD, Gautam VK. Study of Organophosphorus Compound Poisoning in a Tertiary Care Hospital and the Role of Peradeniya Organophosphorus Poisoning Scale as a Prognostic Marker of the Outcome. J Family Med Prim Care 2021;10:4160-7.
21. Pujari KN, Pore NE, Jadkar SP. Serum Enzymes in Organophosphorous Poisoning. J Med Sci Clin Res 2016;4:10771-8.
22. Sangeetha K, Mohandoss R, Deepavarshini P, Shiv Kumar G. Clinical Utility of Creatine Kinase and Lactate Dehydrogenase as Severity Markers of Organophosphorus Compound Poisoning. Eur J Pharm Med Res 2017;4:597-601.
23. Hariprasad S, Alagesa Boopathi C. Biochemical Studies of Human Blood in Patients Affected with Organaphosphate. Res J Med Med Sci 2009;4:461-8.
24. Rabha M, Baruah C, Boro M. Clinical Profile of Acute Organophosphorous Poisoning with Special Reference to Serum Creatine Phosphokinase and Serum Lactate Dehydrogenase Levels as Prognostic Markers: A Tertiary Care Hospital Based Observational Study in North-East India. Int J Med Res Prof 2017;3:83-8.

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