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Original Research Article

A STUDY ON THE PROGNOSTIC SIGNIFICANCE OF SERUM CREATINE PHOSPHOKINASE LEVELS IN ORGANOPHOSPHORUS POISONING

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Abstract

Background: Organophosphorus compounds are important in many parts of the world. Their toxicity and lack of appropriate medical facilities lead to high fatality rates. This study aimed to assess serum creatine phosphokinase (CPK) levels in OP poisoning and determine the correlation between serum creatine phosphokinase (CPK) levels and the severity of OP poisoning. **Material and Methods:** This study included 100 patients admitted to Govt Rajaji Hospital, Madurai, with a history and features of organophosphate poisoning from December 2015 to May 2016. A previously designed proforma was used to collect the demographic and clinical details of the patients. The initial CPK value was determined, and follow-up values were recorded on days 1,4 and 7. Outcomes were classified as survival with or without ventilator assistance and death. **Results:** Of the 100 patients, most poisoning cases occurred in the 19-30 age group (37%). Sixty-seven were male and 33 were female. Suicide is the most common type of exposure. Familial problems were 66% and were identified as the most common cause of OP poisoning. Patients with CPK values between 391-600 had a lower percentage of survival (6%) and a higher percentage of death (16%). Patients with CPK values of > 600 had a 100% mortality rate. There was a significant difference in CPK between the outcomes ($p=0.012$). There was a significant difference in CPK level between the mean initial and final CPK ($p<0.05$). **Conclusion:** Our study shows that respiratory failure in patients with OP compound poisoning can be predicted at admission using simple parameters such as Creatine Phosphokinase (CPK).

INTRODUCTION

Organophosphorus compounds are of considerable importance in many parts of the world. These compounds were discovered a century ago but are still widely used as insecticides worldwide. Poisoning with these substances is the most common cause of inpatient mortality among all poisonings in developing countries such as India. The toxicity of these compounds and the lack of appropriate medical facilities lead to a high fatality rate.[1] According to statistics, nearly 50% of admissions for acute poisoning in emergency departments are due to organophosphate compounds. Their easy accessibility, along with socio-cultural factors, play a considerable role in the selection of organophosphates as a main suicidal agent and are most often preferred by young, economically productive age groups with a case fatality ratio of around 20 per cent.[2]

The WHO Health Organization estimates that approximately 3 million people are exposed to pesticide poisoning every year, with approximately 2,00,000 deaths per year in developing countries. India has the highest incidence of OP poisoning in the world. Nearly 90% of poisoning cases are suicidal, with fatality rates of >10%, 8-10% accidental, and <1% homicidal. Occupational exposure accounts for 1/5th of accidental poisoning cases, with fatalities of <1%.[3,4] A history of exposure and signs of cholinergic overactivity can help in the diagnosis of these poisonings. Treatment includes physiological antagonism with atropine, glycopyrrolate, and oximes, which help reactivate the enzyme. Complications, such as respiratory

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failure, CNS depression, and ventricular arrhythmias, should be anticipated and treated.

Organophosphate poisoning is associated with cardiac complications, most of which occur within the first few hours of exposure. Hypoxemia and electrolyte derangements are major predisposing factors for the development of these complications.[5] The cardiac manifestations of these poisonings include hypotension, hypertension, sinus bradycardia, sinus tachycardia, and cardiac arrest due to arrhythmias. Organophosphates are known to cause myocardial necrosis (myocardiotoxicity). Electrocardiographic changes in organophosphate compound poisoning have been reported, along with associated structural myocardial damage. These complications can be prevented if poisoning is recognised early and treated effectively.[6,7] Organophosphates are not cardiotoxic, and they also influence neural dysfunction and brain damage by altering the normal internal milieu, leading to an altered level of consciousness. The Glasgow Coma Scale is widely used to assess the level of consciousness and to predict the prognosis in patients with cortical dysfunction.[8,9]

Aim

This study aimed to assess serum creatine phosphokinase (CPK) levels in OP poisoning and determine the correlation between serum creatine phosphokinase (CPK) levels and the severity of OP poisoning.

MATERIALS AND METHODS

This study was conducted on 100 patients admitted to the Govt Rajaji Hospital, Madurai, with a history and features of organophosphate poisoning from December 2015 to May 2016. The institutional ethics committee approved the study before initiation, and informed consent was obtained from all patients.

Inclusion Criteria

Patients aged > 18 years with a history of exposure to OP poisoning within 6 hours were included.

Exclusion Criteria

Patients with an indication of exposure to an entirely different poison other than OPC poisoning with OP poisoning and mixed with any other poison who had consumed poison along with alcohol and patients who were chronic alcoholics with a history suggestive of chronic liver disease history suggestive of myopathy history of malignancy and autoimmune diseases history of renal disease history of intake of drugs, such as statins and dexamethasone, were excluded.

Patients with initial high CPK values and those who have a non-declining trend are associated with increased morbidity and mortality and thereby require intensive care monitoring. This might help to predict and assess the prognosis of patients with OP poisoning. A previously designed proforma was used to collect the demographic and clinical details of the patients. The initial CPK value was determined, and follow-up values were recorded on days 1,4 and 7. Initial CPK values and further follow-up values were determined, and they were compared with the severity of poisoning, as suggested by the dosage of atropine and pralidoxime used, as well as the development of complications such as respiratory failure and outcome. Outcomes were classified as survival with or without ventilator assistance and death.

Blood: HB, TC, DC, ESR, ECG, Random blood sugar, Blood Urea, Serum creatinine, Serum creatine kinase, LFT: SGPT and SGOT, and any other relevant investigations if indicated. Use un-hemolysed serum or plasma (EDTA/Heparin), and it is recommended to follow NCCLS procedures. Diagnostic reagent for the quantitative in vitro determination of creatine phosphokinase in human serum and plasma.

Statistical Analysis

The data collected in this study were formulated into a master chart in Microsoft Office Excel, and statistical analysis was performed using the statistical software package SPSS V.17 for Windows.

RESULTS

Of the 100 patients, the majority of poisoning cases occurred in the 19-30 age group (37%). Sixty-seven were male and 33 were female. Suicide was the most common type of exposure in 100 cases. Familial problems were 66% and were identified as the most common cause of OP poisoning. Methyl parathion is the most commonly detected compound. Water consumption (48%) was the most common consumption mode. [Table 1]

Patients with CPK values of < 390 had a higher survival rate (78%). Patients with CPK values between 391-600 had a lower percentage of survival (6%) and a higher percentage of death (16%). Patients with CPK values of > 600 had a 100% mortality rate. There was a significant difference in CPK between outcomes (p=0.012). [Table 2]

If the initial CPK level is high (> 600) in Organophosphorus poisoning, patient mortality is high, and the initial serum CPK level is elevated in acute OPC poisoning if the exclusion of any other disease or conditions may cause an increase in CPK levels. This study was statistically significant, and the p-value was < 0.05. [Table 3]

Table 1: Demographic data of the study

		Number (%)
Age	19-30	37(37%)
	31-40	21(21%)
	41-50	23(23%)

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	51-60	16(16%)
	>60	3(3%)
Sex	Male	63(63%)
	Female	37(37%)
Type of exposure	Accidental	6(6%)
	Intentional	94(94%)
Reason	Familial	66(66%)
	Financial	15(15%)
	ill Health	7(7%)
	Job stress	6(6%)
	Others	6(6%)
Agents	Bug killer liquid	13(13%)
	Chlorpyrifos	9(9%)
	Dichlorofos	4(4%)
	Fenthion	7(7%)
	Monocrotophos	8(8%)
	Methyl parathion	52(52%)
	Quinolphos	7(7%)
Mode of consumption of poison	With Milk	34(34%)
	Others	18(18%)
	With Water	48(48%)

Table 2: Correlation between creatine phosphokinase and patient outcome

CPK	Outcome			P-value
	Survival	Death	Total (%)	
<390	78	0	78(78%)	0.012
391-600	1	5	6(6%)	
>600	0	16	(16%)	

Table 3: Comparison of the initial and final serum creatine phosphokinase levels of patients

CPK level (IU/L)	Initial CPK	Final CPK	P-value
Mild (<390)	225.59±56.301	121.013±27.613	< 0.001
Moderate (390 - 600)	492.667±70.955	1076.33±554.485	0.028
Severe (> 600)	751.18±91.327	1138.18±248.646	< 0.001

DISCUSSION

Organophosphorus (OP) compounds are among agriculture's most commonly used pesticides. OP toxicity is an important global health problem because of its widespread use and easy accessibility, especially in many developing countries. Every year, hundreds of thousands of deaths occur worldwide due to poisoning with OP compounds.[10] Inhibition of acetylcholinesterase is regarded as the major toxic mechanism of OP, which leads to the excessive stimulation of muscarinic and nicotinic receptors. The typical clinical picture of cholinergic crisis develops fast, being the basis for clinical diagnosis, confirmed by the history and demonstration of cholinesterase inhibition.[11] Despite the benefits of acetylcholinesterase monitoring, this test is not available in most parts of the developing world where there is a high caseload of OP poisoning.[12]

In our study, most of the patients manifested with vomiting and abdominal pain (100%), followed by depressed mental status (25%), pinpoint pupil (24%), fasciculation (21%), respiratory failure (21%) and convulsions (10%) Researchers in their study on OP intoxicated patients reported that the most frequent clinical signs were bronchial hypersecretion (52%), tachycardia (47%), meiosis (45%), salivation (41%), and bradycardia (31%).[13] Because increased serum CPK concentration always reflects injury to the tissue of high CPK activity, CPK measurements are particularly useful in diagnosing many medical conditions like acute myocardial and skeletal muscle injuries. Traditional theories relate CPKemia to agitation, hyperactivity, and drugs (rhabdomyolysis and muscle necrosis). The present study showed that there was a high degree of correlation between the initial serum CPK levels and the severity of acute OP poisoning, as illustrated by the positive correlation of initial serum CPK level with (the total dose of atropine in "mg" and pralidoxime in "g"). These correlations were highly significant ($p < 0.001$). These results agree with Bhattacharyya et al., who confirmed a high correlation between initial CPK value and POP scale, serum EChE levels, arterial pH values and total dose of atropine in acute OP poisoning.[14]

Muscle fibre necrosis and, consequently, increased CPK levels occur in severely acute OP-poisoned cases. Therefore, cheaper, easily quantifiable, and more available biochemical markers of OP poisoning, such as serum CPK, can be used to predict and assess the prognosis of patients with OP poisoning.14 The severity of OP poisoning in this study ranged from mild to moderate and severe; most of the cases presented with mild OP toxicity. The authors demonstrated that the POP scale could efficiently predict the severity of OP-poisoned poisoning. Meanwhile, the authors stated that the POP scale uses a high respiratory rate and cyanosis, and this approach is likely to be misleading in

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severe OP poisoning as patients may have either a reduced respiratory rate or tachypnea.[15]

Researchers reported that there was a significant negative linear correlation between the GCS scores and the severity of OP intoxication.[16] On the other hand, the authors stated that BChE measurement on admission has been used to stratify OP poisoning severity.[17] However, it may not be helpful since different OP compounds inhibit BChE to differing degrees compared to their inhibition of the clinically important AChE. Therefore, BChE activity does not always reflect severity and must be interpreted carefully.

In the present study, elevated serum CPK levels were confirmed during the acute toxicity stage, that is, all cases presented within 6 h of exposure to OP compounds and before the development of the intermediate syndrome. This agreed with the authors, who confirmed in their study on OP-intoxicated patients that serum CPK levels are elevated even in the absence of intermediate syndrome, presumably due to muscle fibre necrosis.[14] The intermediate syndrome occurs between the periods of acute and delayed OP toxicity.

The present study highlights the importance of serial measurement of serum CPK levels, as it might help predict and assess the prognosis of patients with acute OP poisoning. Serum CPK levels measured in recovering patients without complications during therapy tended to decrease at follow-up. This agreed with Sahjian and Frakes, who stated that if there is an ongoing injury to the muscle due to the development of complications, the CPK level continues to be elevated since the half-life of CPK is about 1.5 days; it normalises within 5–6 days of a single insult to the muscle.[18]

The present study found that the initial serum CPK level is comparable to the BChE level and can be used as an alternative biomarker to diagnose acute OP poisoning if any other diseases or conditions that may cause a rise in CPK levels are excluded ($p < 0.05$). This agrees with the findings of Perreault et al., who confirmed that CPK leaks into the blood and urine when skeletal muscle is injured. Serum CPK level remains the best biomarker for detecting and monitoring skeletal muscle damage and diseases.[19] Also, the authors confirmed the elevation of serum CPK levels in acute OP poisoning, especially if the patient is severely poisoned, presumably due to muscle fibre necrosis.[14] However, the main disadvantage of serum CPK as a biomarker for acute OP poisoning is its non-specificity. Therefore, the exclusion of other conditions and diseases that may cause its elevation in patients with acute OP poisoning is mandatory.

Our study showed that early respiratory failure occurred soon after admission, while the delayed form occurred several hours to 5 days after admission. The mechanism of respiratory failure will likely involve three components: depression of the central respiratory drive from the respiratory centre, respiratory muscle weakness, and direct pulmonary effects such as bronchorrhea and bronchospasm. Our study showed a direct correlation between initial CPK levels and poisoning severity. Hence, a high initial CPK level can negatively affect patient prognosis.

CONCLUSION

Our study shows that respiratory failure in patients with OP compound poisoning can be predicted at admission using simple parameters, such as Creatine Phosphokinase (CPK). This prognostic parameter can help doctors at peripheral health centres successfully predict outcomes; therefore, high-risk cases are referred to higher centres without delay. Thus, the incidence of complications and mortality associated with OP poisoning could be reduced. The study observed a progressive increase in Creatine Phosphokinase levels with increasing severity of poisoning, reflecting the possible correlation between OPC poisoning and Creatine Phosphokinase levels.

Creatine Phosphokinase levels can be a prognostic marker for OPC intoxication, enabling early detection of severity and identification of those at risk of delayed complications. High CPK levels lead to hypersecretion, depression, miosis, and fasciculation, with a high incidence of respiratory depression and intermediate syndromes. The mean number of days of mechanical ventilation, intensive care stay, and in-hospital stay were correlated with the severity of poisoning. Creatine phosphokinase levels returned to normal after treatment, improving the patient's condition. Optimising the doses and durations of atropine and pralidoxime is crucial for severe cases.

Limitations

Since the study was based on assessing the parameters at admission, none of the patients who developed intermediate syndrome were predicted to develop respiratory failure. This study had some limitations. First, the sample size was small. Hence, generalisation of the study results should be made with caution. The study population included patients seeking medical care in our hospital, which is a tertiary care centre; hence, they may not represent the general population. This was an observational longitudinal study with serial measurements of more informative variables. Therefore, longitudinal studies with large population-based populations are needed to circumvent this limitation.

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REFERENCES

1. Banday T, Desai M, Naik V, Tathineni B. Predictors of morbidity and mortality in organophosphorus poisoning: a case study in a rural hospital in Karnataka, India. N Am J

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Med Sci 2015; 7:259. https://doi.org/10.4103/1947-2714.159331.
2. Amir A, Raza A, Qureshi T, Mahesar GB, Jafferi S, Haleem F, et al. Organophosphate poisoning: Demographics, severity scores and outcomes from national poisoning control centre, Karachi. Cureus 2020. https://doi.org/10.7759/cureus.8371.
3. Karunarathne A, Bhalla A, Sethi A, Perera U, Eddleston M. Importance of pesticides for lethal poisoning in India during 1999 to 2018: a systematic review. BMC Public Health 2021;21. https://doi.org/10.1186/s12889-021-11156-2.
4. Wang L, Wu Y, Yin P, Cheng P, Liu Y, Schwebel DC, et al. Poisoning deaths in China, 2006–2016. Bull World Health Organ 2018; 96:314-326A. https://doi.org/10.2471/blt.17.203943.
5. Besen BAMP. Fluid and electrolyte overload in critically ill patients: An overview. World J Crit Care Med 2015; 4:116. https://doi.org/10.5492/wjccm.v4.i2.116.
6. Jayaprakash N, Geetha S. A study of the ECG changes associated with Organophosphorus compound poisoning. IAIM 2019; 6:69-73. https://iaimjournal.com/wp-content/uploads/2019/02/iaim_2019_0602_121.pdf.
7. Anand S, Singh S, Nahar Saikia U, Bhalla A, Paul Sharma Y, Singh D. Cardiac abnormalities in acute organophosphate poisoning. Clin Toxicol (Phila) 2009; 47:230–5. https://doi.org/10.1080/15563650902724813.
8. Caba I-C, Șteangă V, Dobrin M-E, Jităreanu C, Jităreanu A, Profire B-Ștefania, et al. Clinical assessment of acute organophosphorus pesticide poisoning in pediatric patients admitted to the toxicology emergency department. Toxics 2022; 10:582. https://doi.org/10.3390/toxics10100582.
9. Bodien YG, Barra A, Temkin NR, Barber J, Foreman B, Vassar M, et al. Diagnosing level of consciousness: The limits of the Glasgow Coma Scale total score. J Neurotrauma 2021; 38:3295–305. https://doi.org/10.1089/neu.2021.0199.
10. Akyildiz BN, Kondolot M, Kurtoğlu S, Akin L. Organophosphate intoxication presenting as diabetic keto-acidosis. Ann Trop Paediatr 2009; 29:155–8. https://doi.org/10.1179/146532809X440789.
11. Thiermann H, Zilker T, Eyer F, Felgenhauer N, Eyer P, Worek F. Monitoring of neuromuscular transmission in organophosphate pesticide-poisoned patients. Toxicol Lett 2009; 191:297–304. https://doi.org/10.1016/j.toxlet.2009.09.013.
12. Rajapakse BN, Thiermann H, Eyer P, Worek F, Bowe SJ, Dawson AH, et al. Evaluation of the Test-mate ChE (cholinesterase) field kit in acute organophosphorus poisoning. Ann Emerg Med 2011; 58:559-564.e6. https://doi.org/10.1016/j.annemergmed.2011.07.014.
13. Tsai J-R, Sheu C-C, Cheng M-H, Hung J-Y, Wang C-S, Chong I-W, et al. Organophosphate poisoning: 10 years of experience in southern Taiwan. Kaohsiung J Med Sci 2007; 23:112–9. https://doi.org/10.1016/S1607-551X(09)70385-7.
14. Bhattacharyya K, Phaujdar S, Sarkar R, Mullick OS. Serum creatine phosphokinase: a probable marker of severity in organophosphorus poisoning. Toxicol Int 2011; 18:117–23. https://doi.org/10.4103/0971-6580.84263.
15. Eddleston M, Mohamed F, Davies JOJ, Eyer P, Worek F, Sheriff MHR, et al. Respiratory failure in acute organophosphorus pesticide self-poisoning. QJM 2006; 99:513–22. https://doi.org/10.1093/qjmed/hcl065.
16. Sam KG, Kondabolu K, Pati D, Kamath A, Pradeep Kumar G, Rao PGM. Poisoning severity score, APACHE II and GCS: effective clinical indices for estimating severity and predicting outcome of acute organophosphorus and carbamate poisoning. J Forensic Leg Med 2009; 16:239–47. https://doi.org/10.1016/j.jflm.2008.12.004.
17. Eddleston M, Eyer P, Worek F, Rezvi Sheriff MH, Buckley NA. Predicting outcome using butyrylcholinesterase activity in organophosphorus pesticide self-poisoning. QJM 2008; 101:467–74. https://doi.org/10.1093/qjmed/hcn026.
18. Sahjian M, Frakes M. Crush injuries: Pathophysiology and current treatment. Adv Emerg Nurs J 2007; 29:145–50. https://doi.org/10.1097/01.tme.0000270337.34627.02.
19. Perreault S, Birca A, Piper D, Nadeau A, Gauvin F, Vanasse M. Transient creatine phosphokinase elevations in children: a single-centre experience. J Pediatr 2011; 159:682–5. https://doi.org/10.1016/j.jpeds.2011.03.045.

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