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General Medicine

SERUM CREATINE PHOSPHO KINASE AS PREDICTOR OF INTERMEDIATE SYNDROME IN PATIENT WITH ORGANOPHOSPHOROUS POISONING IN TERTIARY CARE HOSPITAL

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KEYWORDS :

INTRODUCTION

Poisoning is a global public health problem.[1] The World Health Organisation estimates that nearly 250,000 deaths occur globally due to poisoning each year, with pesticides alone causing 150,000 deaths[2]. OP poisoning causes what is known as the "suicide impulse" which leads to high level of suicides in some sectors of the agricultural industry. An estimated 230,000 suicides occur each year in India[3], of whom at least 70,000 (30%) die from pesticide suicide[4]. The commonly encountered OP compounds comprise insecticides (including malathion, parathion, diazinon, fenthion, dichlorvos, chlorpyrifos, ethion), nerve gases (including soman, sarin, tabun, VX), ophthalmic agents (echothiophate, isoflurophate), antihelmintics (such as trichlorfon), herbicides [including tribufos (DEF), merphos which are tricresyl phosphate containing industrial chemicals]. Organophosphate compounds are widely used as pesticides in agricultural parts of the world[5]. Although red blood cell (RBC) cholinesterase and plasma pseudocholinesterase levels can both be used, RBC cholinesterase correlates better with central nervous system. Acetylcholinesterase is, therefore, a more useful marker for organophosphate poisoning[6].

In general, following OP exposure, Salivation, Lacrimation, Urination, Defecation, Gastric cramps, Emesis (SLUDGE) symptoms occur acutely within minutes to hours. Further symptoms and signs may occur as a continuum, wherein patients with acute symptoms involving one neuronal sub-system (e.g. neuromuscular weakness) may progress to develop delayed symptoms and signs of extra-pyramidal system. The third approach, an organ specific approach, have focused on neurologic, respiratory or cardiovascular effects of OP[7-9]. Complications include acidosis, respiratory paralysis, acute renal failure, seizures, arrythmias, aspiration, coma and even death. Intermediate syndrome or type II paralysis usually occurs after 24-96 hours after acute cholinergic crisis. Incidence of Intermediate syndrome varies from 8-50%. Chronic OP poisoning can cause organophosphate-induced delayed neuropathy and is seen mostly in agricultural workers[10].

Laboratory evidence of OP poisoning is usually confirmed by measuring the decreases in the BChE and EChE activities[11]. OP poisoning leads to three main syndromes: Acute cholinergic syndrome, intermediate syndrome and OP induced delayed neuropathy. In OP poisoning, intermediate syndrome manifests between the end of the acute cholinergic crisis and delayed neuropathy. Respiratory paralysis in IMS, if identified early can reduce the need for ventilator support, morbidity, and mortality. Serum creatine phosphokinase is elevated in IMS[12].

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. 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[14].

Serum CPK level can be an efficient biomarker in case of acute OP poisoning not only due to its easy availability and low cost, but also because serial monitoring of its level during the entire course of therapy can predict the prognosis. Serum creatine phosphokinase can be a simple, cheap and widely available biomarker for acute OP poisoning. It can be of particular importance in developing countries, where other costly biomarkers are difficult to estimate[15].

Treatment of OP poisoning consists of intravenous atropine and oximes. The clinical course of OP poisoning may be quite severe and may need intensive care management[16].

AIMS:

Thus the present study was conducted to measure serum creatine phosphokinase levels by Peradeniya scale and to assess progonostic significance of creatine phosphokinase level in assessing the severity of organophosphorus compounds poisioning and to estimate duration of hospital stay, in hospital mortality and atropine/PAM dosage used for control of the OP poisoning.

MATERIALS AND METHODS

An observational cross-sectional study was carried out on a total of 63 patients with OP poisoning who attended the outpatient clinic as well as those admitted in the department of General Medicine at SMS medical college and attached group of hospitals to measure serum creatine phosphokinase (CPK) levels in organophosphorous (OP) insecticide poisoning for a period of one year (January 2020 to June 2021). Written informed consent were obtained from all of the subjects. The study was approved by the Ethics Committee.

The study included patients over 18 years old admitted with organophosphate (OP) poisoning). However, patients with a history of OP poisoning mixed with other poisons, individuals with pre-existing medical conditions such as myopathy, epilepsy, psychiatric illness, autoimmune disease, malignancy, trauma, renal disease, myocardial infarction, myocarditis or recent intramuscular injections were excluded. Furthermore, patients taking certain medications like statins, fibrates, dexamethasone, frusemide, and Amphotericin B, patients admitted more than 48 hours after OP ingestion, those with a history of acute febrile illness within the last month and those unwilling or unable to provide consent were also excluded from the study.

METHODOLOGY:

The study collected baseline clinical characteristics, including demographic, clinical, and biochemical data. A detailed history and physical examination were conducted, assessing vital parameters and systemic examination. Laboratory investigations included venous blood tests for various parameters: hemoglobin, total leukocyte count, differential leukocyte count, prothrombin time, lactate, serum urea, creatinine, electrolytes (sodium, potassium, chlorine), blood sugar, liver enzymes (AST, ALT, ALK phosphatase), amylase, bilirubin, lactate dehydrogenase (LDH), and creatine phosphokinase (CPK) levels.

Estimation Of CPK Level The enzyme creatine kinase catalyses the reaction between creatine phosphate and ADP to creatine and ATP. It is estimated in Kinetic mode using International Federation of Clinical Chemistry (IFCC) methodology. The rate of absorbance change at 340 nm is directly proportional to creatine kinase activity. It is done in a

Semi-automated analyser Model BTS 350. The normal expected values are Males- 46-190 IU/L, Female- 24-165 IU/L at 37 degree C.CPK MB is estimated using same principle used to measure CPK, IFCC methodology in Semi-automated analyser BTS 350. The normal expected value is <25 IU/L at 37 degree C.

Statistical Analysis:
The data was collected in MS Excel 2020 and analyzed using SPSS 20.0. Descriptive statistics were presented as mean ± SD for continuous variables and frequencies for categorical variables. Comparisons were made using Student's t-test for continuous variables and chi-square (x2) analysis for categorical variables.

RESULTS

Table 1

	Frequency (n=63)	Percentage
AGE GROUPS (years)		
<20	8	12.69
20-40	38	60.32
41-60	16	25.40
>60	1	1.59
GENDER		
Female	16	25.40
Male	47	74.60
RESIDENTIAL AREA		
Urban	12	19.00
Rural	51	81.00
OCCUPATION		
Driver	4	6.30
Farmer	22	34.90
Housewife	8	12.70
Labour	9	14.30
Shopkeeper	3	4.80
Student	12	19.00
Teacher	5	7.90

Table 2 : Distribution According To Ionotropic Support Given

	Frequency (n=63)	Percentage
IONOTROPIC SUPPORT GIVEN		
NO	51	81
YES	12	19
INVASIVE VENTILATION PROVIDED		
NO	52	82.5
YES	11	17.5

Table 3:

	MEAN	SD
ATROPINE (mg)	35.4952	16.02791
PAM (mg)	5970.9841	1497.74531

Table 4 : Mean Values Of CPK-NAC, ATROPINE, PAM, Duration Of Hospital Stay With Pop Scale Score

POP Scale Score/ Severity	CPK-NAC		ATROPINE (mg)		PAM (mg)		Duration of stay	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Mild (0-3) [n=27 (42.86%)][Mortality 0 (0%)]	181.59	80.52	22.37	9.84	4575.25	887.84	3.11	1.12
Moderate (4-7) [n=33 (52.38%)] [Mortality 3 (9.09%)]	700.81	1017.15	42.69	8.82	6889.69	772.27	6.12	3.23
Severe (8-11) [n=3 (4.76%)] [Mortality 3 (100%)]	3787.66	1840.14	74.40	2.16	8426.66	692.55	10.33	4.61
	P 0.0021 (S)		0.003 (S)		0.0034 (S)		0.041 (S)	

Table 5: Distribution According To Outcome

OUTCOME	FREQUENCY	PERCENTAGE
EXPIRED	6	9.5
RECOVERED	57	90.5
Total	**63**	**100.0**

DISCUSSION

The present study was conducted at the Department of Medicine, S.M.S Medical College and Hospital, Jaipur, India. The present study was conducted from Jan 2020 to June 2021. The total of 63 male and female patients of >18 years old, presenting with OP poisoning in the General Medicine wards & ICUs were enrolled for the study.

In the present study, maximum 60.32% patients were 20-40 years old, followed by 41-60 years, least being 1.59% aged >60 years. Maximum 74.6% patients were males and 25.4% were females, showing a male predilection. Similar results were observed in a study by **Kumar GC et al.**[12] who also found a male predilection, with a mean age of 31.48±11.76 years. Similarly **Bhattacharyya K et al.**[15] found in their study that out of 63 patients, 42 were men and 21 were women (male:female=2:1). They were aged from 16 to 44 years (mean age=25.5 years). We observed that maximum 81.0% patients belong to rural area and 19.0% belong to urban area. Maximum 34.9% patients are farmers, followed by 19.0% were students, least being 4.8% were shopkeeper. Similar to our study, **Mishra D et al.**[17]80.95% came from a rural background, with a predominantly lower and lower middle socioeconomic status according to the Modified Kuppuswamy Scale. They were mostly farmers by occupation; some others were students, housewives, laborers or porters. Their level of education varied from illiterates to graduates.

The higher the level of toxin in the tissue, more should be the symptoms. Based on this hypothesis a scoring system known Peradeniya organophosphorus poisoning (POP) scale was put forth by **Senanayake et al**[13]. This scale uses 6 clinical parameters to assess the severity of poisoning and thereby decide on the prognosis. Poisoning severity is measured using the Peradeniya Organophosphorus Poisoning (POP) scale. Mortality rates are relatively low for mild to moderate disease. Severe disease as calculated by the POP carries an exceptionally high mortality rate.

We also assessed OP toxicity using POP scale. Out of 63 patients, maximum 52.3% patients had moderate level of severity (4-7), followed by mild (0-3) and severe level (8-11). Out of 63 patients, maximum 60.32% had pin point pupil size, followed by 36.5% patients with <2mm size of pupil and 1.6% each with >2 mm and 2 mm pupil size. All patients with severe poisoning died, 9.09% patients with moderate poisoning had mortality, whereas no patients with mild poisoning had mortality. Out of 63 total patients, 9.52% showed mortality. 90.5% patients recovered and 9.5% expired after OPC poisoning. In contrast to our study **Makwava Prakash V et al.**[18]; in their study noted that a majority of the cases were in the mild group and they attributed it to the higher number of accidental consumption in the group. The numbers in each group was a higher number of mild (50%) POP poisoning, closely followed by moderate poisoning (44%). In study by **Siddraj Wali et al.**[19], assessed the severity of the OPC poisoning was assessed clinically by Peradeniya Organophosphorus Poisoning (POP) scale.

Out of 63 patients, maximum 100% had increased salivation, lacrimation, GI cramps, bronchospasm and bronchorrhea. Minimum patients had signs of cyanosis. Out of 63 patients, maximum 77.8% had no findings and 22.2% had B/L - LZ inflitrates. Out of 63 patients, maximum 9.5% had COPD and DM, minimum had CKD.

The outcomes for patients with respect to mild, moderate and severe disease when calculated by the POP in this study were comparable to previous data by **Amir A et al.**[20] Severe disease had the highest mortality; most cases of severe disease had respiratory complications. The scale is also dynamic. Development of altered level of consciousness or fasciculations or seizures was ominous and portended a guarded prognosis. Many a patient with these signs eventually required mechanical ventilatory support.

In our study, out of 63 patients, maximum 79.4% had no syndrome and 20.6% had intermediate syndrome. Out of 63 patients, maximum

81.0% had no support and 19.0% had IONOTROPIC SUPPORT, maximum 82.5% had no ventilation provided and 17.5% were provided with invasive ventilation. In a study by **Siddraj Wali et al.**[19] 37 (18%) developed the intermediate syndrome, out of them 21 (10 %) recovered and 16 (8 %) patients died. 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.

Since many of these effects are reversed by atropine, early and appropriate medical attention is vital. In developing countries, where OP poisoning is common, quick access to medical care is more problematic than early recognition.

In our study, we also used atropine and PAM for managing OPC poisoning. Mean atropine dose was 35.4952±16.02791 mg. Mean PAM dose was 5970.9841±1497.74531 mg . Mean duration of hospital stay was 5.03±3.19 days. In present study, Mean CPK-MB was 57.0241±31.35578 and mean CPK –NAC was 625.2857±1103.90510. We observed and compared CPK-NAC, atropine, PAM, duration of hospital stay according to POP scale score. Levels of all parameters were found maximum with severe OP poisoning, followed by moderate and mild severity. All parameters showed a decrease with level of severity of OP poisoning. A statistically significant correlation was observed between CPK-NAC levels and Atropine, PAM, Duration of stay and POP scale score. In accordance with our study, **Siddraj Wali et al.**[19] 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**[15], **Nermeen et al**[20] and **Sen R et al.**[21].

Similar to our study, **Raghavendra Mural et al.**[22] the mean CPK levels on day 1 were 183.1, 489.9 (IU/L) in mild and moderate cases of poisoning in our study. Mean CPK levels were 273.53, 456.06, 1032.57 (IU/L) and 89.1, 273 and 688.8 (IU/L) in **Bhattacharyya et al**[15], **Nermeen et al**[20] study respectively. Mean CPK was found to be elevated (2139.8 IU/L) in fatal cases. These results are in consensus with **Bhattacharyya et al**[15]

The present study showed that there was a high degree of correlation between the initial serum CPK levels and the severity of OP poisoning as illustrated by the positive correlation of initial CPK with POP score. This is further supported by D. **Markandeyulu's**[23] and **Kumar et al**[12] study.

John et al[24] and **Kumar et al**[12] concluded that muscle damage determines the subsequent development and severity of intermediate syndrome. In our study, we observed that serum CPK level is elevated even in the absence of intermediate syndrome, provided the patient is severely poisoned. Studies by **Dursun Aygun et al**[25] and **Karalliedde et al**[26] also reported the same.

Organophosphorus compound poisoning is seen in the productive population of males under the age of 40 years, hence there is an urgent need to get control of the situation. But this remains an uphill task which can be done with political commitment and regulation of sales of organophosphorus compound. The Peradeniya score (POP) applied at admission was able to predict the outcome of the subjects in terms of both morbidity and mortality. The results of our study agreed with other study done, which had similar results and hence it is safe to assume that POP score which is an easy, quick and inexpensive method can be used on all patients presenting with OP poisoning as a predictor of outcome.

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, where EChE and BChE levels are not widely available in most of the laboratories. Serial measurements of serum CPK levels in acute OP poisoning can predict the prognosis.

REFERENCES

1. Karunarathne A, Bhalla A, Sethi A. et al. Importance of pesticides for lethal poisoning in India during 1999 to 2018: a systematic review. BMC Public Health. 2021;21:1441.
2. World Health Organization. Guidelines for establishing a poison centre. Geneva:WHO; 2020.
3. Dandona R, Kumar GA, Dhaliwal R et al. Gender differentials and state variations in suicide deaths in India: the global burden of disease study 1990–2016. Lancet Public Health. 2018;3(10):e478–89.
4. Patel V, Ramasundarahettige C, Vijayakumar L et al. Suicide mortality in India: a nationally representative survey. Lancet. 2012;379(9834):2343–51.
5. Peter JV, Sudarsan TI, Moran JL. Clinical features of organophosphate poisoning: A review of different classification systems and approaches. Indian J Crit Care Med 2014;18:735-45.
6. Jeyaratnam J. Acute pesticide poisoning: a major global health problem. World Health Stat Q. 1990; 43(3):139-44.
7. Eddleston M, Mohamed F, Davies JO et al. Respiratory failure in acute organophosphorus pesticide self-poisoning. QJM 2006;99:513-22.
8. Noshad H, Ansarin K, Ardalan MR et al. Respiratory failure in organophosphate insecticide poisoning. Saudi Med J 2007;28:405-7.
9. Anand S, Singh S, Nahar Saikia U et al. Cardiac abnormalities in acute organophosphate poisoning. Clin Toxicol (Phila) 2009;47:230-5.
10. Emerick GL, Peccinini RG, de Oliveira GH. Organophosphorus-induced delayed neuropathy: a simple and efficient therapeutic strategy. Toxicol Lett. 2010; 192(2):238-44.
11. Bansod YV et al. Evaluation of Serum Creatine Phosphokinase as a Marker of Severity in Organophosphorus Poisoning. International Journal of Biomedical Research 2018; 09(05): 179-183.
12. Kumar GC, Bhuvana K, Venkatarathnamma PN et al. Serum creatine phosphokinase as predictor of intermediate syndrome in organophosphorus poisoning. Indian J Crit Care Med. 2015;19(7):384-7.
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. Lokesh NK, Shivakumar KM, Anikethan GV. Serum creatine phosphokinase as predictor of intermediate syndrome in organophosphorus poisoning. International Journal of Contemporary Medical Research 2018;5(6):F1-F4.
15. Bhattacharyya K, Phaujdar S, Sarkar R et al. Serum creatine phosphokinase: a probable marker of severity in organophosphorus poisoning. Toxicol Int. 2011;18(2):117-23.
16. Sungur M, Guven M. Intensive care management of organophosphate insecticide poisoning. Crit Care. 2001;5:211.
17. Mishra D, Singh HP. Kuppuswamy's socioeconomic status scale--a revision. Indian J Pediatr. 2003; 70(3):273-4.
18. Prakash M, Ram O, Harsh DS. Acute Organophosphorus Poisoning And Clinical Admission Score Association Among Patients Admitted In Emergency Ward Of A Tertiary Teaching Hospital Of Medical College. Journal of Pharmaceutical and Biomedical Sciences (JPBMS). 2012;17(08):1-5.
19. Siddraj Wali, Basavaraj GT. Prognostic significance of creatine phospokinase (CPK) levels in assessing the severity of organophosphorus poisoning compound poisoning. MedPulse International Journal of Medicine. September 2020;15(3):64- 68.
20. Nermeen AM, 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;4:18–29.
21. 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.
22. 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 2017;4(2):578-582.
23. Markandeyulu D. The Study of Serum Creatine Phosphokinase (Cpk) as s Marker of Severity in Organophosphorous Poisoning in Comparison with Pseudocholinesterase Levels. Biomirror. 2015;6.
24. 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.
25. Aygun D, Erenler AK, Karatas AD et al. Intermediate syndrome following Acute Organophosphate poisoning: Correlation with initial Serum levels of Muscle Enzymes. Basic Clin Pharmacol Toxicol. 2007;100:201-4.
26. Karalliedde L, Baker D, Marrs TC. OrganophosphateInduced Intermediate Syndrome. Toxicological Reviews. 2006;25:1-4.