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Study of Serum Creatine Phosphokinase in Patients of Organophosphorous Poisoning and Its Correlation with the Severity of Organophosphorous Poisoning

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ABSTRACT

OBJECTIVE-

To estimate the serum levels of Creatine phosphokinase in acute organophosphorus poisoning cases.

To assess serum creatine phosphokinase level correlation with severity of organophosphorus poisoning.

METHODS- The observational study was carried out on 50 patients above the age of 17 years presenting with organophosphorus poisoning admitted in Emergency Ward (EW) of medicine department at Tertiary Health Center, South Gujarat.

RESULT-The POP score, Serum cholinesterase levels and serum creatine phosphokinase levels showed a significant association in predicting the need for ventilatory support. Lower grade of poisoning had a better outcome whereas higher severity of poisoning had a poorer outcome.

CONCLUSION-The elevated creatine kinase is commonly seen in OP compound poisoning and associated with high morbidity and higher mortality. High Serum levels of creatine kinase at admission indirectly indicate the severity of poisoning and poor prognosis.

KEY WORDS: Organophosphorus poisoning, Serum creatine phosphokinase

I. INTRODUCTION

Acute poisoning by Organophosphosphorous insecticide (OP) has reached epidemic proportions in most parts of the world, particularly in developing countries like India, where agriculture is the backbone. Their ease of access and socio–cultural factors play important role in choice of OP as a self-poison and the incidence is higher among young economically active group with a common fatality ratio of 20%. Insecticide compounds has caused many numbers of suicidal deaths all over India [1]. OP poisoning causes what is called the "suicide impulse" which leads to high level of suicides in some sectors of the agricultural industry. According to the World Health Organization (WHO), 1 million serious unintentional poisonings occur every year and an additional 2 million people are hospitalized for suicide attempts with pesticides [2]. The commonly encountered OP compounds comprising of insecticides (such as malathion, parathion, diazinon, fenthion, dichlorvos, chlorpyrifos, ethion), nerve gases (such as soman, sarin, tabun, VX), ophthalmic agents (echothiophate, isoflurophate), antihelmintics (such as trichlorfon), herbicides [including tribufos (DEF), merphos such as tricresyl phosphate containing industrial chemicals].They act by inhibiting the acetylcholinesterase enzyme (AchE) at muscarinic and nicotinic receptors, producing an array of symptoms like miosis, bradycardia, increased gastrointestinal motility, emesis, sweating, tachypnoea, salivation, lacrimation, altered sensorium, fasciculation, bronchospasm, blurred vision, photophobia, urination and defecation. Complications of op poisoning include acidosis, respiratory paralysis, acute renal failure, seizures, arrhythmias, aspiration, coma and even death. OP poisoning leads to three main syndromes: Acute cholinergic syndrome, intermediate syndrome (IMS), and OP induced delayed neuropathy (OPIDN). [3] IMS occurs 48–96 h after ingestion of OP compound and following recovery from the acute cholinergic crisis, characterized by skeletal muscle weakness. Respiratory paralysis in IMS if

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identified early can reduce the need for ventilator support and appropriate treatment can be initiated at the earliest. [4] The causes of death in OP poisoning may be either one or a combination of the above. Early diagnosis is a key to cure. A delay of initiation of treatments limits not only outcome, but also the opportunity to use 2-PAM (cholinesterase re-activator) which prevents "aging" of the enzyme. Till now, investigations were comprised of serum erythrocyte cholinesterase (EchE) and plasma cholinesterase (PchE) estimation, the levels of which are reduced in OP poisoning. But these are costly and not regularly performed in most laboratories of our country. Besides, the kinetic study of inhibition of human AchEs by Demeton-S-methyl has shown that cholinesterase-based titration methods are not suitable for the estimation of Ops. [5] There are emerging options for newer, cheaper and/or easily quantifiable biochemical markers to determine the severity in OP poisoning like creatine phosphokinase (CPK), lactate dehydrogenase (LDH), serum immunoglobulins (IgG, IgA), circulating complements (C3, C4), etc. [6] But the immunoglobulin assays – IgG, IgA, are costly and difficult to perform in most laboratories, are often unreliable. Several animal model studies conducted on rat liver and fresh-water snails have indicated the association between OP poisoning and CPK levels. [7] In a study, it was proposed that serum level of CPK is often found to be elevated in OP poisoning and may be used as a biomarker. There will be the elevation of serum CPK in OP poisoning due to myonecrosis caused by persistent depolarization at the neuromuscular junction and oxidative cellular damage to muscle membrane. [8] Serum CPK level has also been studied as a predictor for the onset of IMS. With this background in mind, we are undertaking a study to assess the role of CPK as an alternative prognostic marker and to establish a correlation between CPK levels and the severity of OP poisoning.

II. MATERIAL AND METHODS –

The study was conducted among indoor patients admitted to our tertiary care hospital.

1. Study Design- observational, cross sectional analytical study
2. Inclusion Criteria -

Patients who meet all the following criteria were included in the study-

a. Patients > 18 years
b. Patients with history of exposure to OP poisoning within 24 hours

3. Exclusion Criteria (All / any of the following)-

a. Patients having age less than 18 years.
b. History of Mixed poisoning
c. History suggestive of Myopathy, Epilepsy, Psychiatric illness, Autoimmune disease, Malignancy, Trauma, Sepsis, Renal disease, Myocardial infarction and Myocarditis, recent IM injection.
d. History of drug intake like statins, dexamethasone, frusemide and amphotericin B.

III. OBSERVATION-

The results of this study which included 50 patients were as follows: -

TABLE 1: DISTRIBUTION OF PATIENTS ACCORDING TO THEIR GENDER

GENDER	NO.	PERCENTAGE (%)
Male	24	48
Female	26	52
Total	50	100

In the present study conducted, 48% of the patients were males and 52% of the patients were females.

TABLE 2: DISTRIBUTION OF PATIENTS ACCORDING TO TYPE OF ORGANOPHOSPHOROUS COMPOUND CONSUMED

TYPE OF O.P. CONSUMED	NO. OF PATIENTS	PERCENTAGE (%)

Malathion	8	16
Endosulphan	8	16
Methyl parathion	8	16
Chlorpyriphos	11	22
Diazinon	7	14
Dichlorvos	8	16

In this study most commonly used poison was chlorpyriphos upto 22 % of total patients followed by Dichlorvos, Endosulphan, malathion, diazinon and Methyl parathion each having value of 16% of total patients.

TABLE 3: DISTRIBUTION OF PATIENTS ACCORDING TO THEIR PRESENTING SYMPTOMS

SYMPTOMS	NO. OF PATIENTS	PERCENTAGE (%)
Vomiting	43	86
Nausea	36	72
Salivation	36	72
Sweating	35	70
Bronchorhea	28	56
Lacrimation	25	50
Breathlessness	25	50
Diarrhoea	20	40
Convulsion	11	22
Diplopia	8	16

In this study, the most common symptom reported by patients was vomiting (86%) followed by other common symptoms like nausea (72%), Salivation in 72% and excessive sweating in 70% patients.

TABLE 4: DISTRIBUTION OF PATIENTS ACCORDING TO THEIR CLINICAL SIGNS

SIGNS	No. of patients	Percentage (%)
Miosis	47	94
Bradycardia	34	68
Respiratory rate	33	66
Fasciculation	18	36
Neck muscle weakness	17	34
Altered consciousness	12	24
Convulsion	10	20
Cyanosis	8	16

In this study, the most commonly found clinical sign was miosis in 94% of patients followed by bradycardia which was seen in 68 % of patients and respiratory involvement was seen in 66 % of patients.

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TABLE 5: ASSOCIATION BETWEEN QUANTITY OF POISON CONSUMED AND MORTALITY

QUANTITY	NO. OF PATIENTS	EXPIRED	SURVIVED	
<30	15	0	15	p value <0.002
30-50	17	0	17	
>50	18	6	12	
*chi square test applied p value <0.002				

None of patients expired in this study who consumed up to 50 ml of poison. 6 patients who expired out of 18 consumed more than 50ml of poison. This result was statistically significant
(p **value <0.002).**

TABLE 6: OUTCOME OF PATIENTS

OUTCOME	NO. OF PATIENTS	PERCENTAGE (%)
Survived	44	88
Expired	6	12
Total	50	100

In our study mortality was 12% and survival rate was 88%.

TABLE 7: COMPARISON OF SEVERITY ACCORDING TO POP SCORE V/S SERUM CHOLINESTERASE LEVELS (IU/L)

POP SCORE	SERUM CHOLINESTERASE LEVELS (IU/L)			
	>4200	1681-4200	841-1680	<840
0-3 (MILD)	7	12	8	1
4-7(MODERATE)	0	6	5	5
8-11 (SEVERE)	0	0	0	6
NO. OF PATIENTS	7	18	13	12

TABLE 8: COMPARISON BETWEEN POP SCORE AND MEAN SERUM CREATINE PHOSPHOKINASE LEVELS (IU/L) (n=50)

POP SCORE	MEAN OF SERUM CREATINE PHOSHPHOKINASE	Std.Dev. of SERUM CRETINE PHOSPHOKINASE	NO. OF PATIENTS	P-value <0.0001
0-3	77.14	23.63	28	
4-7	386.56	286.36	16	
8-11	788.66	216.25	6	

***ANOVA P-VALUE <0.0001**

The mean serum CPK levels are not same among the different levels of POP score. The mean S.CPK levels were in lower range with mild POP score and were in higher range with increasing severity of POP score. This result was statistically significant (**PVALUE <0.0001).**

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TABLE 9: COMPARISON OF PATIENTS ACCORDING TO SEVERITY OF SERUM CHOLINESTERASE WITH SERUM CREATINE PHOSPHOKINASE

GRADE	CHOLINESTERASE ACTIVITY	SERUM CHOLINESTERASE (IU/L)	SERUM CREATINE PHOSPHOKINASE(IU/L)	
			NORMAL	ABNORMAL
			29-195	>195
Normal	>50%	>4200	7	0
Mild	20-50%	1680-4200	15	3
Moderate	10-20%	840-1680	9	4
Severe	<10%	<840	2	10

As the severity of O.P. poisoning increases, there is decrease in cholinesterase levels with subsequent decrease in its activity, there was a rise in S. CPK levels. This was a statistically significant.

TABLE 10: SHOWING ASSOCIATION BETWEEN POP SCORE, SERUM CREATINE PHOSPHOKINASE LEVELS, SERUM CHOLINESTERASE LEVELS AND OUTCOME

POP SCORE	MEAN OF SERUM CREATINE PHOSPHOKINASE (IU/L)	MEAN OF SERUM CHOLINESTERASE(IU/L)	EXPIRED	SURVIVED
0-3	77.14 (± 23.63)	2930 (± 1533.4)	0	28
4-7	386.56 (± 286.36)	1404 (± 716.05)	2	14
8-11	788.66 (± 216.25)	373 (± 157.76)	4	2

Chi square test p value <0.00003 with the increasing severity of O.P poisoning, there was subsequent rise in S.CPK Levels and decrease in serum cholinesterase levels which was associated with increasing mortality rates. In our study, the result was statistically significant (p value <0.00003).

IV. DISCUSSION-

A total 50 no. of cases were studied. The clinical and diagnostic findings of this study were compared with other studies in literature here.

TABLE 11: COMPARING MALE TO FEMALE RATIO IN VARYING STUDIES

SEX	PRESENT STUDY	SHANKAR P. S. et al [13]	A. GOEL et al [10]
Female	52%	59.87%	60%
Male	48%	40.20%	40%
M : F	0.92:1	1.48:1	2.5:1

In present study, out of 50 patients, 48% were males and 52% were females. The male to female ratio in this study is 0.92:1. In other similar study gender distribution reported by Shankar et al(1.48:1) and A Goel et al(2.5:1).

TABLE 12: COMPARISON OF SYMPTOMATOLOGY IN VARYING STUDIES.

SYMPTOMS	PRESENT STUDY	REIHMAN et al [11]	APN KUMAR et al [19]	GOEL et al [10]	KUMAR et al [20]

Vomiting	86%	80%	93%	97.08%	62.50%
Salivation	72%	32%	85%	28.15%	36.25%
Sweating	70%	-	-	-	36.25%
Nausea	72%	-	-	-	77.50%
Lacrimation	50%	-	80.60%	-	7.50%

In the present study, vomiting was the commonest symptom seen in 86%, followed by nausea (72%) and Salivation (72%). In other study almost similar findings were seen.

TABLE 13: COMPARISON OF CLINICAL SIGNS IN VARYING STUDIES

CLINICAL SIGNS	PRESENT STUDY	REIHMAN et al [11]	A GOEL et al [10]	APN KUMAR et Al [19]	KUMAR et al [20]
Miosis	94%	60%	95%	62%	93.75%
Fasciculation	36%	8%	55%	38.60%	65%
Tachypnoea	66%	34%	42.50%	81.30%	73.50%
Bradycardia	68%	52%	-	39%	27.50%
Altered sensorium	24%	30%	75%	-	25%

The common clinical signs were miosis (94%), tachypnoea (66%), Fasciculations (36%). These results are comparable to the studies of Reihman et al [11], A Goel et al [10], APN Kumar et al [19] and Kumar et al [20].

TABLE 14: COMPARISON OF MORTALITY IN VARYING STUDIES.

STUDY	MORTALITY
PRESENT STUDY	12%
DAS B. WET et al [21]	13.30%
ARUP KUMAR KUNDU et al [22]	13.30%
NOIURA et al [23]	10%
REIHMAN et al [11]	14%

In present study, mortality of 12%. which is in comparison with Das. B.Wet al [21](13.3%),Arup kumar kundu et al [22](13.3%), Noiura et al [23](10%), Reihman et al [11](14%). 100% of patients with mild grade of poison according to POP scale survived. 2 out of 6 patients who had expired had moderate grade and 4 patients expired out of 6 who had severe grade of poisoning according to POP scale. POP scale had a statistically significant correlation with mortality. (p value < 0. 00003).

TABLE 15: COMPARISON OF S.CPK IN VARYING STUDIES.

	S. CPK LEVELS (MEAN ± SD)	
	PRESENT STUDY	BHATTACHARYA et al [24]

MILD (0-3)	77.14(± 23.63)	273.53 (± 108.71)
MODERATE (4-7)	386.56 (± 286.36)	456.06 (± 77.02)
SEVERE (8-11)	788.66 (± 216.25)	1032.57 (± 205.65)

In our study, there is positive correlation between CPK and POP score (r=0.8393). These results are in correlation with **Bhattacharyya et al [24]** who confirmed the presence of a high degree of correlation between initial CPK value and POP scale. Muscle fiber necrosis and consequently increase in CPK levels occur in severely acute OP poisoned cases. So, cheaper, easily quantifiable and more available biochemical markers in relation to OP poisoning like serum CPK, serum amylase, serum lactate dehydrogenase etc. can be used in predicting and assessing the prognosis of patients with OP poisoning.

V. CONCLUSION

The elevated creatine kinase is commonly seen in OP compound poisoning and associated with high morbidity and higher mortality. We also concluded that higher the clinical grade of poisoning at initial presentation, more is the incidence of respiratory failure and need for mechanical ventilator support. High Serum levels of creatine kinase at admission indirectly indicate the severity of poisoning and poor prognosis. Early estimation of creatine kinase should be routinely considered as it is a good prognostic marker as well as marker in intermediate syndrome with cost benefits and easy availability.

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