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Original Research Article

Study of serum creatinine phosphokinase and serum lactate dehydrgenase as prognostic markers in organophosphorus poisoning

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ABSTRACT

Background: Organophosphorus (OP) compounds are insecticides which are widely used in agriculture. Acute organophosphorus poisoning is an important cause of morbidity and mortality in developing countries like India. In a limited resourced country like India, we need cheap and easily measurable biomarkers for predicting prognosis.
Objective was to estimate creatinine phosphokinase and serum lactate dehydrgenase as prognostic markers in acute organophosphorus poisoning.
Methods: Total 94 cases of OP poisoning admitted to KIMS Hospital, Hubbali between January 1st 2017 to December 31th 2017 were studied. Detailed history, clinical examination and lab investigations like pseudo cholinesterase, serum LDH and serum CPK were carried out. Peradeniya OP poisoning scale was applied to all study subjects and the severity of OP poisoning was graded as mild, moderate, severe. Data obtained was analysed by different statistical methods.
Results: OP poisoning is more common in adults of age group between 20 - 30 years, Incidence is was more in male patients, Mortality rate is 12.8%. Mean values of serum LDH, serum CPK were negatively correlated with pseudcholinesterase levels and it was statistically significant. Correlation between the severity of OP poisoning (based on Peradenyia score) and biochemical parameters like serum CPK, serum LDH, was statistically significant.
Conclusions: The correlation between the severity of OP poisoning and biochemical parameters was statistically significant and they are usefull in predicting development of respiratory failure.

Keywords: CPK, LDH, Organophosphorus poisoning, Pseudo cholinesterase, Peradenyia score

INTRODUCTION

Acute poisoning is an important cause of morbidity and mortality in developing countries like India. In medical emergency 10% of admissions are due to poisoning and organophosphorus poisoning contributes to nearly 50% of it.[1] Accidental poisoning may occur due to inhalation while spraying insecticide for crops, while self-poisoning is always by ingestion to commit suicide. Using insecticide compounds as a mean to end life is grouped under nonviolent methods for suicide. Unemployment, failure in examination, social economical, and domestic problems are all increasing creating psychological stress to the victims. Such stress stimulates these people to consume these OP poisons due to its low price, high availability and high toxicity.

In our country these compounds are most often are misused as suicidal agents. Since 1963 the incidence of OP poisoning is in a steady rise in India.[2] The exact rate of OP poisoning in India is not clear because of under reporting and lack of data. India is an agricultural country

and OP compounds are used greatly for the agriculture in India. Therefore, the access to these harmful pesticide substances is so easy. In many reports from India, rate of suicidal poisoning with OP compounds ranges from 10 to 43%.[3] The morbidity and mortality in these patients depends on the time lag between the exposure and the onset of management. So, it is very important to recognise the whole spectrum of symptoms in OP poisoning.

The need for newer biomarkers in relation to OP poisoning started a very long time ago. OP labelled albumin in plasma, blood beta-glucuronidase and paraxonase status were suggested by some scientists to be very reliable marker for both diagnosis of the poisoning and prognosis. But these assays are not available widely are very costly. In a limited resourced country like India, we need cheap and easily measurable biomarkers. Many studies were conducted regarding this and were shown that Serum cholinesterase can be a useful tool in the diagnosis of OP poisoning. But its role in prognostication is very minimal. A number of recent studies were conducted using parameters like liver enzymes, serum amylase and serum Creatine phosphokinase(CPK) as newer markers and their correlation with severity and prognosis of OP poisoning.[2,4,5] This study was conducted to assess parameters like Creatinine Phosphokinase and serum lactate dehydrgenase as to predict the severity and prognosis in OP poisoning patients.

METHODS

OP poisoning patients those getting admitted in department of Medicine, KIMS hospital, Hubbali, during the period of January 1st 2017 to December 31th 2017 are taken up for Prospective observational study considering the inclusion and exclusion criteria. Total number of patients studied 94.

Inclusion criteria

A history of exposure to organophosphorus compound within previous 24 hours with characteristic clinical manifestations of organophosphorus compound poisoning.

Exclusion criteria

- Patients with indication of exposure to an entirely different poison other than OP poison
- Patients with OP poisoning and mixed with any other poison
- Patients who have consumed poison along with alcohol
- Patients who are chronic alcoholic
- Patients with Ultrasound abdomen suggestive of Acute Pancreatitis
- Patients with history suggestive of gall stone disease / parotid gland disease / lipid disorders / renal / hepatic disease / Diabetes Mellitus.

Method of collection of data

When the patient was admitted in our hospital, with history of exposure to organophosphorus compound within previous 24 hours, informed consent was obtained. A thorough clinical examination was carried out with particular reference to vital parameters, pupil size, fasciculation's, neck muscle weakness, salivation, lacrimation, sweating, assessment of central nervous system, respiratory system and cardiovascular system as per prescribed Performa.

This examination took place during initial resuscitation and treatment of the patient. Peradeniya OP poisoning scale was applied to all study subjects and the severity of OP poisoning was graded as mild, moderate, severe. About 5ml of blood was collected in plain tube under aseptic precautions. The blood was allowed to clot and serum was separated by centrifugation and used for the analysis.

All patients were managed with decontamination procedure including gastric lavage. Intravenous atropine 2-4mg bolus and repeated every 5-15minutes initially until atropinisation. The end point of treatment was taken as the drying up of secretions. The atropinisation was maintained for 24-48 hours with intermittent doses, every 15-30 minutes or depending on the need, and then tapered over days depending upon patient's response. Pralidoxime chloride was given to all patients as 2g IV bolus over 10-15minutes immediately after admission and 0.5g-1.0g IV 6th hourly for 48hours depending on patient's condition.

Patients were kept under strict observation during their stay in hospital. Assessment of patient's airway and need for endotracheal intubation was assessed. Patients with respiratory failure were intubated and mechanical ventilator support was given.

Investigations

Complete blood count, Liver function test, Serum lactate dehyrdrogenase, Renal function test, Serum amylase, Random blood sugar, Electrocardiogram, Serum pseudocholinesterase, Serum creatine Phosphokinase, Ultrasound abdomen, Lipid Profile.

Statistical analyses

All the patient characteristics are summarised as frequencies and percentages. All biochemical parameters are summarised as mean, median, standard deviation (SD) and range. Mean Biochemical parameters are compared with categories of pseudo cholinesterase and Peradenyia score using chi square test. All the biochemical parameters are compared with respiratory failure and outcome using ANOVA or student t test. The p value was considered significant if it is less than 0.05.

RESULTS

In the present 50% of the patients ware in age group between 21-30. Next common age group was between 31-40 (17%) and 15% were in less than 21 years of age. In this study with a total participant of 94 patients, 50 of them are male (53.2%) and 44 of them are female (46.8%).

In this study majority of the patients are Farmers and Daily wage workers (each 23%) and house wife (22.3%). Most of the patients are from rural area. Suicidal intention was the most common cause of poisoning. Only 8(8.5%) are due to accidental poisoning. Commonest compound ingested is Monochrotophos 17% followed by Dichlorovas 13.8%, Chlorpyriphos 12.8%, Profenofos 8.5%, Dimehthoate 7.4%.

In about 20 patients (21.3%) compound was not known. The most common symptom reported by patients in our study was vomiting (89.4%), followed by salivation/lacrimation/sweating (56.4%) loose stools (34.04%) dyspnea (35.10%) and Altered sensorium (31.9%). Seizures was present only in 9 patients (9.6%).

Miosis was the most common sign (87%) noted in this study followed by Bradycardia in 67% Neck muscle weakness in 43.6% Tachypnea in 42.6%, Fasciculations in 37.2%, Crepitations in 36.2% and altered sensorium in 31.9% of patients. Most of the patients were in mild group (45%) followed by moderate group (35%) and Severe group (20%). 36 patient (38.3%) had respiratory failure. Mortality rate in this study was 12.8% (12 patients).

In the present study out of 94 patients 22 were in mild group, 34 were in moderate group and 38 patients had severe reduction of pseudo cholinesterase level. The mean Serum LDH value is 581.91, 672.18 and 1153.17 in mild, moderate and severe Pseudo cholinesterase groups respectively. p value is <0.0001 and it is statistically significant and thus serum LDH showed statistically significant negative correlation (p <0.0001) with pseudo cholinesterase (Table 1).

Table 1: Comparison of LDH across different pseudo cholinesterase categories.

Category	(N=)	Mean	SD	Median	Minimum	Maximum	p value
Mild	22	195.59	105.8	166.5	103	553	<0.0001
Moderate	34	309.41	123.27	293.5	120	673	
Severe	38	615.68	344.32	523.5	117	1562	

Table 2: Comparison of CPK across different pseudo cholinesterase categories.

Category	(N=)	Mean	SD	Median	Minimum	Maximum	p value
Mild	22	112.45	23.91	114.5	81	182	0.008
Moderate	34	109.56	24.1	111.5	75	165	
Severe	38	156.66	69.65	152	65	314	

Table 3: Comparison of LDH across different Peradeniya categories.

Category	(N=)	Mean	SD	Median	Minimum	Maximum	p value
Mild	42	222.83	110.39	191.5	103	553	
Moderate	33	407.82	152.77	374	188	873	<0.0001
Severe	19	810.63	358.89	756	397	1562	

The mean CPK value is 195.59, 309.59 and 615.68 in mild, moderate and severe Pseudocholinesterase groups respectively. P value is <0.0001 and it is statistically significant and thus serum CPK levels showed statistically significant negative correlation (p <0.0001) with pseudo cholinesterase (Table 2). The mean Serum LDH value is 583.48, 812 and 1482.89 in mild, moderate and severe Peradenyia groups respectively. Serum LDH showed a high degree of positive correlation with Peradeniya score and the correlation was also statistically significant (p <0.0001) (Table 3).

The mean Serum CPK value is 222.83, 407.82 and 810.63 in mild, moderate and severe Peradenyia groups respectively. Serum CPK level showed a high degree of positive correlation with Peradeniya score and the correlation was also statistically significant (p <0.0001) (Table 4).

The association between the severity of OP (based on Peradenyia score) and other biochemical parameters showed that there was statistically significant association with respect to CPK, LDH.

Table 4: Comparison of CPK across different Peradeniya categories.

Category	(N=)	Mean	SD	Median	Minimum	Maximum	p value
Mild	42	111.93	23.35	115.5	75	182	
Moderate	33	121.39	48.4	113	65	291	0.0013
Severe	19	181.32	72.7	179	68	314	

Table 5: Distribution of respiratory failure based on different biochemical parameter categories and Peradenyia Score.

		Absent	Percentage	Present	Percentage	p value
Peradeniya score	Mild	42	(100.0)	0	(0.0)	
	Moderate	29	(87.9)	4	(12.1)	<0.001
	Severe	11	(57.9)	8	(42.1)	
CPK level	Upto 195	23	(100.0)	0	(0.0)	0.03
	>195	59	(83.1)	12	(16.9)	
LDH level	230-460	10	(100.0)	0	(0.0)	0.2
	>460	72	(85.7)	12	(14.3)	

In the present study respiratory failure was present in all the patients (100%) in severe Peradenyia group and 51.5% in Moderate group none in mild group. And also 84.2% of patients in severe pseudocholinesterase group and only 4% in moderate group and none in mild group. When Serum CPK is elevated respiratory failure was present in 50.7% and none of the patients with normal CPK level had respiratory failure. Similarly elevated LDH is associated with respiratory failure in 41.7% cases (Table 5).

DISCUSSION

In present study, majority of patients were in the age group of 21-30 years (50%). Totally 84.1% of patients were within 40 years of age. This finding corresponds with the results of studies carried out by workers Prasad et al, A Goel et al.[6,7]

This study revealed a slight male preponderance (53.2%), females accounting for 46.8% of cases. The male to female ratio in this study is 1.13:1. This corresponds to gender distribution reported by Rajeev H et al, A Goel et al.[7,8] In this study most of the patients were from rural area (67%), urban patients constitute only 33%. This finding was similar to that of Gupta et al.[9]

In the present study most of the patients were in mild group (45%) followed by moderate group (35%) and Severe group (20%). Makwava PV et al, 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.[10] Closely followed by moderate poisoning (44%).

In the study conducted by Dubey TN et al, severity of OP poisoning as per POP scale ranged from mild to severe, most of the cases 68% belonged to mild grade of poisoning, 27% of the patients belonged to moderate grade and only 5% of patients had severe grade of poisoning.[11]

Table 6: Peradeniya organophosphorus poisoning (POP) scale.

Parameter		Score
Miosis	Pupil size >2mm	0
	Pupil size ≤2mm	1
	Pupils pin point	2
Fasciculations	None	0
	Present but not generalized or continuous	1
	Generalized and continuous with central cyanosis	2
Respiration	Respiratory rate ≤20/min	0
	Respiratory rate >20/min	1
	Respiratory rate >20/min with central cyanosis	2
Bradycardia	Pulse rate >60/min	0
	Pulse rate 41-60/min	1
	Pulse rate ≤40/min	2
Level of consciousness	Conscious and rational	0
	Impaired, responds to verbal commands	1
	Impaired, no response to verbal commands (if convulsion present add 1)	2
Total		11

In the present study respiratory failure was present in all the patients in severe peradeniya group and none in the mild group, among moderate group 51.5% patients had repiratory failure. Out of 12 deaths 8 were in severe and 4 were in moderate Peradenyia group.

These findings are consistent with Dubey TN et al, Makwava PV et al.[10,11] In the present study out of 94 patients 22 were in mild group, 34 were in moderate group and 38 patients had severe reduction of pseudocholinesterase level (PChE).

PChE level at presentation is a reliable indicator of the severity of OP poisoning and a predictor of respiratory failure and mortality. Similar findings were reported by Chaudry SC et al, Hiremath P et al.[12,13]

In the present study serum CPK levels showed statistically significant negative correlation ($p < 0.0001$) with pseudocholinesterase, high degree of positive correlation with Peradeniya score and the correlation was also statistically significant. The association between the severity of OP (based on Peradenyia and pseudocholinesterase levels) and serum CPK was statistically significant.

When Serum CPK is elevated respiratory failure was present in 50.7% and none of the patients with normal CPK level had respiratory failure. Only 16.9% patents with elevated serum CPK level have died this was not statistically significant. Similar results were observed in the studies done by K. Bhattacharya et al, D. Markandeyulu et al, and T N Dubey et al.[5,14]

In Raghvendra et al, study high initial CPK level is associated with need for endotracheal intubation and mechanical ventilation and more chances of mortality.[15] Dayanand Raddi et al, reported that the elevation of CPK levels is predictive of subsequent respiratory failure.[16]

It is known that serum CPK levels increases in muscle injury and is used as an indicator in muscle injury. High serum CPK activity shows the magnitude of acute muscle necrosis. The presence of muscle fiber necrosis in OP poisoning has already been demonstrated in animal experiments by Calore et al.[17] The present study found that the initial serum CPK level is comparable for pseudocholinesterase level and can be used as an alternative biomarker in diagnosis of acute OP poisoning, However, the main disadvantage of serum CPK as a biomarker for acute OP poisoning, its non-specificity. So, exclusion of other conditions and diseases that may cause its elevation of CPK in patients with acute OP poisoning is mandatory.

In this study serum LDH showed statistically significant negative correlation with pseudocholinesterase, and high degree of positive correlation with Peradeniya score. The association between the severity of OP (based on Peradenyia and Pseudo cholinesterase levels) and serum LDH was statistically significant. When Serum LDH is elevated respiratory failure was present in 41.7% and only one patient with normal LDH had respiratory ailure. The serum LDH between survivors and non-survivors was not statically significant.

S. Hariprasad et al, have found increased LDH activity in serum of patients with organophosphorus poisoning.[18] In S. Agarwal et al, study serum LDH activity was significantly elevated ($p \leq 0.01$) in poisoning cases indicating muscular functional impairment due to organophosphorus toxicity.[2] Sangeetha et al, Serum LDH levels can be an efficient biomarker in case of acute OP poisoing.[19] In Rabhani M et al, study serum Lactate Dehydrogenase levels, however, did not correlate in predicting mortality in poisoning cases.[20]

CONCLUSION

This study concludes that the correlation between the severity of OP poisoning (based on Pseudo cholinesterase) and biochemical parameters like serum CPK, serum LDH, was statistically significant and they are useful in predicting development of respiratory failure.

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