Original Research Article

Study the prognostic significance of various biochemical parameters in organophosphorus poisoning

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Abstract

Background: Acute organophosphorus poisoning is an important cause of morbidity and mortality in developing countries like India. **Objective:** To study clinical features and biochemical parameters in patients admitted with acute organophosphorus poisoning and to determine use of these biochemical marker in prediction of severity of acute OP poisoning. **Material and method:** 94 cases of OP poisoning admitted to KIMS Hospital, Hubbali between January 1st 2017 to December 31th 2017 were studied. **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 amylase, serum LDH, serum CPK and serum creatinine 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 pseudocholinesterase, serum amylase, serum CPK, serum LDH, RBS was statistically significant. But Serum Creatinine levels did not show statistically significant correlation. **Conclusions:** The correlation between the severity of OP poisoning and biochemical parameterswas statistically significant and they are usefull in predicting development of respiratory failure.

Keywords: Amylase, CPK, LDH, Serum creatinine, RBS, Organophosphorus poisoning, Peradenyia score.

Introduction

In the developing world, Poisoning is a common method of suicide. Pesticide poisoning is a major health hazard in the developing world[1].

Millions of people are exposed to these dangerous chemicals because of the occupational hazards and also because of unsafe storage practices[2]. However it is the deliberate self poisoning that causes majority of the deaths and a difficult health strategy to manage among health services, especially in Asia[3]. 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[4]. 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.

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[5]. 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%[6]. Among these patients mortality rate is as high as 20 to 70%[7].

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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 and 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[8].Our study was conducted to assess parameters like serum pseudocholinesterase, serum lactate dehydrgenase (LDH), serum CPK, serum amylase, random blood sugar (RBS) and serum creatinine to predict the severity and prognosis in OP poisoning patients.

Material and method

94 cases of 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. Ethical clearance was obtained from the institutional ethical committee for the present study

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 a 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.

Method of collection of data

Informed consent was obtained with history of exposure to organophosphorus compound within previous 24 hours. 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.

Detailed history, clinical examination and lab investigations like pseudocholinesterase, serum amylase, serum LDH, serum CPK, RBS and serum creatinine 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.

Statistical analysis

All biochemical parameters are summarised as mean, median, standard deviation(SD) and range. Mean Biochemical parameters are compared with categories of pseudocholinesterase and Peradenyia score using chi square test. 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%). In this study with a total participants 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%). In this study most of the patients are from rural area. In this study suicidal intention was the most common cause of poisoning. Only 8(8.5%) are due to accidental poisoning. 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%) dyspnoea(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. In the present study most of the patients were in mild group (45%) followed by moderate group (35%) and Severe group (20%). In the present study 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 pseudocholinesterase level.

The mean Serum LDH value is 581.91, 672.18 and 1153.17 in mild, moderate and severe Pseudocholinesterase 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 pseudocholinesterase.

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 pseudocholinesterase.The mean RBS is 112.45, 109.56 and 156.66 in mild, moderate and severe Pseudocholinesterase groups respectively. P value is <0.05 and it is statistically significant and thus RBS levls showed statistically significant negative correlation (P 0.008) with pseudocholinesterase.

The mean Serum creatinine value is 0.836. 0.815 and 1.03 in mild, moderate and severe Pseudocholinesterase groups respectively. P value is 0.017 and it is statistically significant and thus serum creatinine showed statistically significant negative correlation (P <0.05) with pseudocholinesterase.

The mean Serum amylase value is 75.6, 145.76 and 232.37 in mild, moderate and severe Peradenyia groups respectively. Serum Amylase showed a high degree of positive correlation with Peradeniya score and the correlation was also statistically significant (p <0.0001).

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).

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).

The mean blood sugars value is 111.93, 121.39 and 181.32 in mild, moderate and severe Peradenyia groups respectively. Blood sugar levels showed a high degree of positive correlation with Peradeniya score and the correlation was also statistically significant (p 0.0013).

The mean Serum Creatinine value is 0.8, 0.9 and 1.1 in mild, moderate and severe Peradenyia groups respectively. Serum creatinine showed a positive correlation with Peradeniya score and the correlation was also statistically significant (p <0.0013).

Table 1: Comparison of pseudocholinesterase level with various biochemical parameters and Peradenyia score

	Mild		Moderate		Severe		P value
	N	%	N	%	N	%	
Peradeniya score level							
mild	22	(52.4)	17	(40.5)	3	(7.1)	<0.001
moderate	0	(0.0)	17	(51.5)	16	(48.5)	
severe	0	(0.0)	0	(0.0)	19	(100.0)	
Amylase level							
Up to 220	22	(27.8)	32	(40.5)	25	(31.6)	<0.001
>220	0	(0.0)	2	(13.3)	13	(86.7)	
CPK level							
Up to 195	15	(65.2)	7	(30.4)	1	(4.3)	<0.001
>195	7	(9.9)	27	(38.0)	37	(52.1)	
LDH level							
230-460	5	(50.0)	4	(40.0)	1	(10.0)	0.05
>460	17	(20.2)	30	(35.7)	37	(44.0)	

RBS level							
70-140	21	(30.0)	31	(44.3)	18	(25.7)	0.0005
>140	1	(4.2)	3	(12.5)	20	(83.3)	
Creatinine level							
0.5-1.5	22	(24.4)	34	(37.8)	34	(37.8)	0.001
>1.5	0	(0.0)	0	(0.0)	4	(100.0)	

In the present study association between the severity of OP (based on pseudocholinesterase) and other biochemical parameters showed that there was significant negative correlation with respect to amylase, CPK, LDH, RBS and Serum creatinine levels. When compared to Peradenyia score also there was significant correlation.

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 Pseudocholinesterase, amylase, CPK, LDH, RBS. But Serum Creatinine levels did not show statistically significant correlation.

Table 2: Comparison of Peradeniya score with various biochemical parameters

	Mild		Moderate		Severe		P value
	N	%	N	%	N	%	
Choline esterase level							
mild reduction	22	100.0	0	0.0	0	0.0	
moderate reduction	17	50.0	17	50.0	0	0.0	<0.001
severe reduction	3	7.9	16	42.1	19	50.0	
Amylase level							
Up to 220	42	53.2	28	35.4	9	11.4	<0.001
>220	0	0.0	5	33.3	10	66.7	
CPK level							
Up to 195	22	95.7	1	4.3	0	0.0	
>195	20	28.2	32	45.1	19	26.8	<0.001
LDH level							
230-460	9	90.0	1	10.0	0	0.0	0.009
>460	33	39.3	32	38.1	19	22.6	
RBS level							
70-140	39	55.7	26	37.1	5	7.1	<0.001
>140	3	12.5	7	29.2	14	58.3	
Creatinine level							
0.5-1.5	42	46.7	31	34.4	17	18.9	0.14
>1.5	0	0.0	2	50.0	2	50.0	

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. In comparison to Serum amylase all the patients with elevated amylase level had repiratory failure and only 26.6% with normal amylase group had respiratory failure. 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. Blood sugars was elevated in 24 cases out of which 18 patients(75%) had respiratory failure. Only 4 patients had elevated serum creatinine all of them had respiratory failure.

Table 3: Distribution of outcome based on Peradeniya score and different biochemical parameter categories

	Absent	%	Present	%	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)	
Choline esterase level					
mild reduction	22	(100.0)	0	(0.0)	
moderate reduction	34	(100.0)	0	(0.0)	<0.001
severe reduction	26	(68.4)	12	(31.6)	
Amylase level					
Up to 220	72	(91.1)	7	(8.9)	0.009
>220	10	(66.7)	5	(33.3)	
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)	
Random Blood sugar					
70-140	66	(94.3)	4	(5.7)	0.0005
>140	16	(66.7)	8	(33.3)	
Serum Creatinine					
0.5-1.5	81	(90.0)	9	(10.0)	
>1.5	1	(25.0)	3	(75.0)	0.0013

In the present study out of 12 deaths 8 were in severe and 4 were in moderate Peradenyia group. When compared to pseudocholinesterase all 12 deaths were in severe group. In patients with elevated amylase and RBS levels death was seen in 33.3%. Out of 4 patients who had elevated serum creatinine 3 patients died. These associations were statistically significant but the association between death and serum LDH and CPK was not significant.

Discussion

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%) dyspnoea(35.10%) and Altered sensorium(31.9%). Seizures were reported only in 9 patients (9.6%). These findings correlates with the studies done by Edwin J et al[9] and Rajeev H et al[10] .

Miosis was the most common sign (87%) noted in this study. Similarly In the study conducted by Chintale KN et al [11], most common physical finding was Miosis found in 97 patients (71.32%) Followed by fasciculation (63.23%), increased bronchiolar secretions (39.70%), bradycardia (57.35%), altered sensorium (5.88%), neck muscle weakness (16.91%). Similar trend was noted in studies done by Edwin J et al[9].

Peradeniya score

In the present study most of the patients were in mild group (45%) followed by moderate group (35%) and Severe group (20%). Makwava Prakash V et al[12] , 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. Closely followed by moderate poisoning (44%).

In the study conducted by T N Dubey et al[13] 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.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 T N Dubey et al[13] and Makwava Prakash V et al[12].In the present study 36 patient (38.3%) had respiratory failure. Similar findings was shown in other studies. Mortality rate in this study was 12.8%(12 patients). Similar mortality rate was reported by Eddleston et al[14], and Eddleston[15] et al 2006–2015 reported 33.3% mortality rate.

Pseudocholinesterase levels

Based on the pseudocholinesterase levels at the time of admission, subjects were divided into three groups[16]. (Normal range 4,900 – 11000 U/L).

- Mild < 10% reduction (> 4410).
- Moderate 10- 50% reduction (4410- 2450).
- Severe >50% reduction (<2450).

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).

In Giridhar Patil et al. [16] study 82 patients were enrolled. Out of which 51 patients (62.20%) were admitted with mild poisoning, 7 patients were (8.54%) were admitted with moderate poisoning and 24 patients (29.27%) were admitted with severe poisoning.

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[17].Our study results are in accordance with the study done by Lin CL et al., where they found that mean amylase levels were elevated in patient with respiratory failure and serum amylase levels predicted ventilator support in OP poisoning. In Sumathi et al[18] study serum amylase, was negatively correlated with plasma cholinesterase levels. There was significant association with severity of OP poisoning(based on serum pseudocholinesterase) with respect to amylase. In a study conducted in Japan by Sumiya et al, an increase in plasma amylase levels above the normal range have been found in 50% of the patients who developed respiratory failure.

Dressel et al[19] showed that OP intoxication causes increase in intraductal pressure and increase in exocrine pancreas flow rate resulting in extravasation of fluid.

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[8].

In Raghvendra et al [20] study high initial CPK level is associated with need for endotracheal intubation and mechanical ventilation and more chances of mortality. Dayanand Raddi et al[21] reported that the elevation of CPK levels is predictive of subsequent respiratory failure. 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[22]. 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.

S. Hariprasad et al [23] has found increased LDH activity in serum of patients with organophosphorus poisoning. In S.Agarwal et al[5] , study serum LDH activity was significantly elevated ($p \leq 0.01$) in poisoning cases indicating muscular functional impairment due to organophosphorus toxicity. In this study 25.5% of patient had blood sugars levels >140 mg/dl, this was in consistent with Shobhaet al [24] (26%). The association between the severity of OP (based on Peradenyia and Pseudocholinesterase levels) and serum blood sugars was statistically significant.

The association between the severity of OP (based on Peradenyia and Pseudocholinesterase levels) and serum creatinine was statistically significant. Only 4 patients had elevated serum creatinine all of them had respiratory failure, and 3 patints expired. In Naqvi R[25] study on Acute kidney injury from different poisonous substances,184 cases of AKI developing after poisoning were seen. The largest group was from paraphenyline diamine poisoning comprising 135 patients, followed by methanol in 8, organophosphorus compounds in 5. In K.Swaminathan [26] study there was progressive increase in blood urea and serum creatinine levels from mild to severe poisoning.

Conclusion

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

Among the biochemical parameters pseudocholinesterase, serum amylase, RBS, and serum creatinine are usefull to predict the outcome of the patient.

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